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(71) Applicant *(for all designated States except US)*: PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: BROWN, Matthew, Frank [US/US]; 66 Greenhaven Road, Pawcatuck, CT 06379 (US). KATH, John, Charles [US/US]; 252 Shore Road, Waterford, CT 06385 (US). POSS, Christopher, Stanley [US/US]; 10 Hermitage Drive, Gales Ferry, CT 06335 (US).

(74) Agents: SPIEGEL, Allen, J. et al.; Pfizer Inc., Patent Dept., 235 East 42nd Street, New York, NY 10017 (US).

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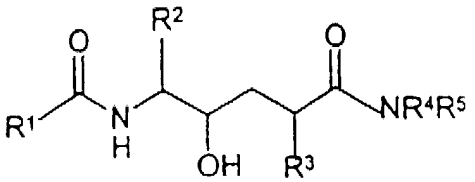
(54) Title: HETEROARYL-HEXANOIC ACID AMIDE DERIVATIVES, THEIR PREPARATION AND THEIR USE AS SELECTIVE INHIBITORS OF MIP-1-ALPHA BINDING TO ITS CCR1 RECEPTOR

(57) Abstract

Compounds of formula (I) wherein R^1 is optionally substituted (C_2-C_9)heteroaryl; R^2 is optionally substituted phenyl-$(CH_2)_m$-, naphthyl-$(CH_2)_m$-, (C_3-C_{10})cycloalkyl-$(CH_2)_m$-, (C_1-C_6)alkyl or (C_2-C_9)heteroaryl-$(CH_2)_m$-, m is an integer from zero to four; R^3 is hydrogen, or optionally substituted (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl-$(CH_2)_n$-, (C_2-C_9)heterocycloalkyl-$(CH_2)_n$-, (C_2-C_9)heteroaryl-$(CH_2)_n$- or aryl-$(CH_2)_n$-, n is an integer from zero to six; or R^3 and the carbon to which it is attached form an optionally substituted and/or fused five to seven membered carbocyclic ring; R^4 is hydrogen, (C_1-C_6)alkyl, hydroxy, (C_1-C_6)alkoxy, hydroxy (C_1-C_6)alkyl, (C_1-C_6)alkoxyCO, (C_3-C_{10})cycloalkyl-$(CH_2)_p$-, or optionally substituted (C_2-C_9)heterocycloalkyl-$(CH_2)_p$-, (C_2-C_9)heteroaryl-$(CH_2)_p$-, phenyl-$(CH_2)_p$- or naphthyl-$(CH_2)_p$-, p is an integer from zero to four; or R^4 and R^5 together with the nitrogen atom to which they are attached form an optionally substituted (C_2-C_9)heterocycloalkyl group; R^5 is hydrogen, (C_1-C_6)alkyl or amino. The present compounds are potent and selective inhibitors of MIP-1-alpha. binding to its receptor CCR1, and are thus useful to treat inflammation and other immune disorders.



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HETEROARYL-HEXANOIC ACID AMIDE DERIVATIVES, THEIR PREPARATION AND THEIR USE AS SELECTIVE INHIBITORS OF MIP-1.ALPHA. BINDING TO ITS CCR1 RECEPTOR

Background of the Invention

The present invention relates to novel hexanoic acid derivatives, methods of use and pharmaceutical compositions containing them.

The compounds of the invention are potent and selective inhibitors of MIP-1α binding to its receptor CCR1 found on inflammatory and immunomodulatory cells (preferably leukocytes and lymphocytes). The CCR1 receptor is also sometimes referred to as the CC-CKR1 receptor. These compounds also inhibit MIP-1α (and the related chemokine shown to interact with CCR1 (e.g., RANTES and MCP-3)) induced chemotaxis of THP-1 cells and human leukocytes and are potentially useful for the treatment or prevention of autoimmune diseases (such as rheumatoid arthritis, type I diabetes (recent onset), inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis), acute and chronic inflammatory conditions (such as osteoarthritis, adult Respiratory Distress Syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, and glomerulonephritis), allergic conditions (such as asthma and atopic dermatitis), infection associated with inflammation (such as viral inflammation (including influenza and hepatitis) and Guillian-Barre), transplantation tissue rejection (chronic and acute), organ rejection (chronic and acute), atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases (including sarcoidosis, leprosy and tuberculosis).

MIP-1α and RANTES are soluble chemotactic peptides (chemokines) which are produced by inflammatory cells, in particular CD8+ lymphocytes, polymorphonuclear leukocytes (PMNs) and macrophages, J.Biol. Chem., 270 (30) 29671-29675 (1995). These chemokines act by inducing the migration and activation of key inflammatory and immunomodulatory cells. Elevated levels of chemokines have been found in the synovial fluid of rheumatoid arthritis patients, chronic and rejecting tissue transplant patients and in the nasal secretions of allergic rhinitis patients following allergen exposure (Teran , et al., J. Immunol., 1806-1812 (1996), and Kuna et al., J. Allergy Clin. Immunol. 321 (1994)). Antibodies which interfere with the chemokine/receptor interaction by neutralizing MIP1α or gene disruption have provided direct evidence for the role of MIP-1α and RANTES in disease by limiting the recruitment of monocytes and CD8+ lymphocytes (Smith et al., J. Immunol, 153, 4704 (1994) and Cook et al., Science, 269, 1583 (1995)). Together this data demonstrates that CCR1 antagonists would be an effective at treatment of several immune based diseases. The compounds described within are potent and selective antagonists of CCR1. No other small molecule antagonists of the MIP-1α /RANTES interaction with CCR1 are currently known.

United States Patent 4,923,864, issued May 8, 1990, refers to certain heterocyclic hexanamides that are useful for treating hypertension.

PCT publication WO 89/01488, published February 23, 1989, refers to renin inhibiting peptides which possess nonpeptide linkages.

PCT publication WO 93/ 025057, published February 4, 1993, refers to dipeptide analogs which are claimed to inhibit retroviral proteases.

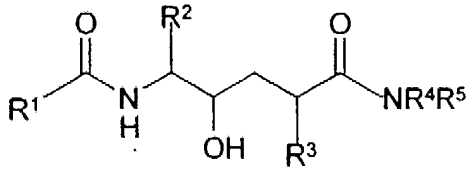
PCT publication WO 93/17003, published September 2, 1993, refers to other dipeptide analogs which are claimed to inhibit retroviral proteases.

PCT publication WO 92/17490, published October 15, 1992, refers to peptides containing at least one O-phosphate monoester or diester. The compounds are claimed to possess activity for inhibiting retroviruses.

European Patent Publication 708,085, published April 24, 1996, refers to antiviral ethers of aspartate protease inhibitors.

Summary of the Invention

The present invention relates to compounds of the formula



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wherein R^1 is $(C_2\text{-}C_9)$heteroaryl optionally substituted with one or more substituents (preferably one to three substituents) independently selected from the group consisting of hydrogen, halo, CN, $(C_1\text{-}C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), $(C_1\text{-}C_6)$alkoxy$(C_1\text{-}C_6)$alkyl, HO-(C=O)-, $(C_1\text{-}C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl-O-(C=O)-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl-(C=O)-O-, $(C_1\text{-}C_6)$alkyl-(C=O)-O-$(C_1\text{-}C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl(O=C)-, $(C_1\text{-}C_6)$alkyl(O=C)-$(C_1\text{-}C_6)$alkyl, NO_2, amino, $(C_1\text{-}C_6)$alkylamino, $[(C_1\text{-}C_6)\text{alkyl}]_2$amino, amino$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkylamino$(C_1\text{-}C_6)$alkyl, $[(C_1\text{-}C_6)\text{alkyl}]_2$amino$(C_1\text{-}C_6)$alkyl, H_2N-(C=O)-, $(C_1\text{-}C_6)$alkyl-NH-(C=O)-, $[(C_1\text{-}C_6)\text{alkyl}]_2$N-(C=O)-, H_2N(C=O)-$(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkyl-HN(C=O)-$(C_1\text{-}C_6)$alkyl, $[(C_1\text{-}C_6)\text{alkyl}]_2$N-(C=O)-$(C_1\text{-}C_6)$alkyl, H(O=C)-NH-, $(C_1\text{-}C_6)$alkyl(C=O)-NH, $(C_1\text{-}C_6)$alkyl(C=O)-

[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

R^2 is phenyl-(CH_2)$_m$-, naphthyl-(CH_2)$_m$-, (C_3-C_{10})cycloalkyl-(CH_2)$_m$-, (C_1-C_6)alkyl or (C_2-C_9)heteroaryl-(CH_2)$_m$-, wherein m is an interger from zero to four, wherein each of said phenyl, naphthyl, (C_3-C_{10})cycloalkyl or (C_2-C_9)heteroaryl moieties of said phenyl-(CH_2)$_m$-, naphthyl-(CH_2)$_m$-, (C_3-C_{10})cycloalkyl-(CH_2)$_m$- or (C_2-C_9)heteroaryl-(CH_2)$_m$- groups may optionally be substituted with one or more substituents (preferably one to three substituents) independently selected from hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, phenoxy, benzyloxy, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

R^3 is hydrogen, (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl-(CH_2)$_n$-, (C_2-C_9)heterocycloalkyl-(CH_2)$_n$-, (C_2-C_9)heteroaryl-(CH_2)$_n$- or aryl-(CH_2)$_n$-; wherein n is an interger from zero to six;

wherein said R^3 (C_1-C_{10})alkyl group may optionally be substituted with one or more substituents, (preferably from one to three substituents) independently selected from hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl,

$(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, $H_2N(C=O)$-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$ N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl; and wherein any of the carbon-carbon single bonds of said $(C_1$-$C_{10})$alkyl may optionally be replaced by a carbon-carbon double bond;

wherein the $(C_3$-$C_{10})$cycloalkyl moiety of said R^3 $(C_3$-$C_{10})$cycloalkyl-$(CH_2)_n$- group may optionally be substituted by one to three substitutents independently selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, $H_2N(C=O)$-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl HN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

wherein the $(C_2$-$C_9)$heterocycloalkyl moiety of said R^3 $(C_2$-$C_9)$heterocycloalkyl-$(CH_2)_n$- group may contain from one to three heteroatoms independently selected from nitrogen, sulfur, oxygen, >S(=O), $>SO_2$ or $>NR^6$, wherein said $(C_2$-$C_9)$heterocycloalkyl moiety of said $(C_2$-$C_9)$heterocycloalkyl-$(CH_2)_n$- group may optionally be substituted on any of the ring carbon atoms capable of forming an additional bond (preferably one to three substitutents per ring) with a substituent independently selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl,

$(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

wherein the $(C_2$-$C_9)$heteroaryl moiety of said R^3 $(C_2$-$C_9)$heteroaryl-$(CH_2)_n$- group may contain from one to three heteroatoms independently selected from nitrogen, sulfur or oxygen, wherein said $(C_2$-$C_9)$heteroaryl moiety of said $(C_2$-$C_9)$heteroaryl-$(CH_2)_n$- group may optionally be substituted on any of the ring carbon atoms capable of forming an additional bond (preferably one to three substitutents per ring) with a substituent selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl; and

wherein said aryl moiety of said R^3 aryl-$(CH_2)_n$- group is optionally substituted phenyl or naphthyl, wherein said phenyl and naphthyl may optionally be substituted with from one to three substituents independently selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-

(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkyl HN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

or R^3 and the carbon to which it is attached form a five to seven membered carbocyclic ring, wherein any of the carbon atoms of said five membered carbocyclic ring may optionally be substituted with a substituent selected from the group consisting of hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl; wherein one of the carbon-carbon bonds of said five to seven membered carbocyclic ring may optionally be fused to an optionally substituted phenyl ring, wherein said substitutents may be independently selected from hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-

$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)alkyl]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)alkyl]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)alkyl]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)alkyl]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)alkyl]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

R^4 is hydrogen, $(C_1$-$C_6)$alkyl, hydroxy, $(C_1$-$C_6)$alkoxy, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy(C=O)-, $(C_3$-$C_{10})$cycloalkyl-$(CH_2)_p$-, $(C_2$-$C_9)$heterocycloalkyl-$(CH_2)_p$-, $(C_2$-$C_9)$heteroaryl-$(CH_2)_p$-, phenyl-$(CH_2)_p$-, or naphthyl-$(CH_2)_p$-, wherein p is an integer from zero to four; wherein said $(C_2$-$C_9)$heterocycloalkyl, $(C_2$-$C_9)$heteroaryl, phenyl and naphthyl groups of said $(C_2$-$C_9)$heterocycloalkyl-$(CH_2)_p$-, $(C_2$-$C_9)$heteroaryl-$(CH_2)_p$-, phenyl-$(CH_2)_p$-, or naphthyl-$(CH_2)_p$- may be optionally substituted on any of the ring atoms capable of supporting an additional bond (preferably zero to two substituents per ring) with a substituent selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$ alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)alkyl]_2$ amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino $(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)alkyl]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)alkyl]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)alkyl]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)alkyl]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

or R^4 and R^5 together with the nitrogen atom to which they are attached form a $(C_2$-$C_9)$heterocycloalkyl group wherein any of the ring atoms of said $(C_2$-$C_9)$heterocycloalkyl group may optionally be substituted, preferably from zero to two substituents, with a substituent selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy,

hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6) alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$ amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino (C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

R^5 is hydrogen, (C_1-C_6)alkyl or amino;

R^6 is hydrogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy-(CH_2)$_g$-, (C_1-C_6)alkoxy(C=O)-(CH_2)$_g$-, (C_1-C_6)alkyl-(SO_2)-(CH_2)$_g$-, (C_6-C_{10})aryloxy-(CH_2)$_g$-, (C_6-C_{10})aryloxy(C=O)-(CH_2)$_g$-, or (C_6-C_{10})aryl-(SO_2)-(CH_2)$_g$-, wherein g is an integer from zero to four;

with the proviso that when one of R^4 or R^5 is hydrogen, and the other of R^4 or R^5 is (C_1-C_6)alkyl; R^2 is (C_3-C_{10})cycloalkyl or isopropyl and R^3 is (C_3-C_5)alkyl, phenyl, methylvinyl, dimethylvinyl, halovinyl, hydroxy(C_1-C_3)alkyl or amino(C_1-C_4)alkyl then R^1 must be other than indol-5-yl, 6-azaindol-2-yl, 2,3-dichloro-pyrrol-5-yl, 4-hydroxyquinolin-3-yl, 2-hydroxyquinoxalin-3-yl, 6-azaindolin-3-yl, or optionally substituted indol-2 or 3-yl;

and the pharmaceutically acceptable salts of such compounds.

The present invention also relates to the pharmaceutically acceptable acid addition salts of compounds of the formula I. The acids which are used to prepare the pharmaceutically acceptable acid addition salts of the aforementioned base compounds of this invention are those which form non-toxic acid addition salts, i.e., salts containing pharmacologically acceptable anions, such as the hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate, bisulfate, phosphate, acid phosphate, acetate, lactate, citrate, acid citrate, tartrate, bitartrate, succinate, maleate, fumarate, gluconate, saccharate, benzoate, methanesulfonate, ethanesulfonate, benzenesulfonate, p-toluenesulfonate and pamoate [i.e., 1,1'-methylene-bis-(2-hydroxy-3- naphthoate)]salts.

The invention also relates to base addition salts of formula I. The chemical bases that may be used as reagents to prepare pharmaceutically acceptable base salts of those compounds of formula I that are acidic in nature are those that form non-toxic base salts with such compounds. Such non-toxic base salts include, but are not limited to those derived from

such pharmacologically acceptable cations such as alkali metal cations (e.g., potassium and sodium) and alkaline earth metal cations (e.g., calcium and magnesium), ammonium or water-soluble amine addition salts such as N-methylglucamine-(meglumine), and the lower alkanolammonium and other base salts of pharmaceutically acceptable organic amines.

The compounds of this invention may contain olefin-like double bonds. When such bonds are present, the compounds of the invention exist as cis and trans configurations and as mixtures thereof.

Unless otherwise indicated, the alkyl and alkenyl groups referred to herein, as well as the alkyl moieties of other groups referred to herein (e.g., alkoxy), may be linear or branched, and they may also be cyclic (e.g., cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl) or be linear or branched and contain cyclic moieties. Branched groups such as 2-methylbutyl, 2-methylpentyl are defined such that the lowest number is the carbon furthest from the point of attachment. Unless otherwise indicated, halogen includes fluorine, chlorine, bromine, and iodine.

(C_3-C_{10})Cycloalkyl when used herein refers to cycloalkyl groups containing zero to two levels of unsaturation such as cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, 1,3-cyclohexadiene, cycloheptyl, cycloheptenyl, bicyclo[3.2.1]octane, norbornanyl etc..

(C_2-C_9)Heterocycloalkyl when used herein refers to pyrrolidinyl, tetrahydrofuranyl, dihydrofuranyl, tetrahydropyranyl, pyranyl, thiopyranyl, aziridinyl, oxiranyl, methylenedioxyl, chromenyl, isoxazolidinyl, 1,3-oxazolidin-3-yl, isothiazolidinyl, 1,3-thiazolidin-3-yl, 1,2-pyrazolidin-2-yl, 1,3-pyrazolidin-1-yl, piperidinyl, thiomorpholinyl, 1,2-tetrahydrothiazin-2-yl, 1,3-tetrahydrothiazin-3-yl, tetrahydrothiadiazinyl, morpholinyl, 1,2-tetrahydrodiazin-2-yl, 1,3-tetrahydrodiazin-1-yl, tetrahydroazepinyl, piperazinyl, chromanyl, etc. One of ordinary skill in the art will understand that the connection of said (C_2-C_9)heterocycloalkyl rings is through a carbon or a sp^3 hybridized nitrogen heteroatom.

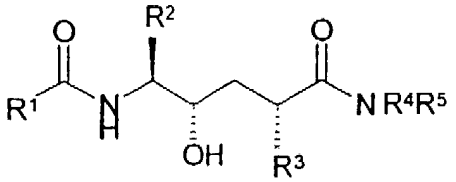
(C_2-C_9)Heteroaryl when used herein refers to furyl, thienyl, thiazolyl, pyrazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrrolyl, triazolyl, tetrazolyl, imidazolyl, 1,3,5-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,3-oxadiazolyl, 1,3,5-thiadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, 1,2,4-triazinyl, 1,2,3-triazinyl, 1,3,5-triazinyl, pyrazolo[3,4-b]pyridinyl, cinnolinyl, pteridinyl, purinyl, 6,7-dihydro-5H-[1]pyrindinyl, benzo[b]thiophenyl, 5, 6, 7, 8-tetrahydro-quinolin-3-yl, benzoxazolyl, benzothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, thianaphthenyl, isothianaphthenyl, benzofuranyl, isobenzofuranyl, isoindolyl, indolyl, indolizinyl, indazolyl, isoquinolyl, quinolyl, phthalazinyl, quinoxalinyl, quinazolinyl, benzoxazinyl; etc. One of ordinary skill in the art will

understand that the connection of said (C_2-C_9)heterocycloalkyl rings is through a carbon atom or a sp^3 hybridized nitrogen heteroatom.

Aryl when used herein refers to phenyl or naphthyl.

The compounds of this invention include all conformational isomers (e.g., cis and trans isomers) and all optical isomers of compounds of the formula I (e.g., enantiomers and diastereomers), as well as racemic, diastereomeric and other mixtures of such isomers.

Preferred compounds of the of formula I include those with the stereochemistry depicted in formula



Ia

Preferred compounds of the formula I include those wherein R^1 is optionally substituted pyrazolo[3,4-b]pyridinyl, cinnolinyl, pyridinyl, 6,7-dihydro-5H-[1]pyrindinyl, benzothiazolyl, indolyl, pyrazinyl, benzoimidazolyl, benzofuranyl, benzo[b]thiophenyl, naphthalenyl, quinoxalinyl, isoquinolinyl, 5,6,7,8-tetrahydro-quinolin-3-yl or quinolinyl, more preferably pyrazolo[3,4-b]pyridin-5-yl, cinnolin-4-yl, pyridin-2-yl, 6,7-dihydro-5H-[1]pyrindin-3-yl, benzothiazol-2-yl, indol-2-yl, pyrazin-2-yl, benzoimidazol-2-yl, benzofuran-2-yl, benzo[b]thiophen-2-yl, naphthalen-2-yl, quinoxalin-2-yl, quinoxalin-6-yl, isoquinolin-1-yl, isoquinolin-3-yl, isoquinolin-4-yl, 5,6,7,8-tetrahydro-quinolin-3-yl, quinolin-2-yl, quinolin-3-yl, quinolin-4-yl or quinolin-6-yl, most preferably quinoxalin-6-yl, quinolin-2-yl, quinolin-3-yl, quinoxalin-2-yl, quinolin-4-yl or quinolin-6-yl.

Other preferred compounds of formula I include those wherein R^2 is optionally substituted phenyl, benzyl, naphthyl, cyclohexyl, thienyl, thiazolyl, pyridyl, oxazolyl, furanyl, or thiophenyl; wherein said substituents are independently selected from hydrogen, halo, (C_1-C_6)alkyl, trifluoromethyl, trifluoromethoxy, hydroxy, -C(=O)-OH, (C_1-C_6)alkoxy, (C_1-C_6)alkoxy(C=O)-, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, phenoxy, and benzyloxy.

Other preferred compounds of formula I include those wherein R^3 is optionally substituted (C_1-C_{10})alkyl, benzyl, pyranyl or (C_3-C_{10})cycloalkyl-(CH_2)$_n$-, wherein any of the carbon-carbon single bonds of said (C_1-C_{10})alkyl may be optionally replaced by a carbon-carbon double bond; more preferably optionally substituted n-butyl, t-butyl, 2-methylpropyl, 2-methylbutyl, 3-methylbutyl, n-pentyl, 2-methyl-pentyl, allyl, cyclopentyl, cyclohexyl 2-methylcyclohexyl, cyclohexylmethyl, or cycloheptyl, more preferably wherein the substituent is fluoro, (C_1-C_6)alkyl or hydroxy.

Examples of specific preferred compounds of the formula I are the following:

7,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

8-fluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-1(S)-(3-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(2-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(2,6-dimethyl-tetrahydro-pyran-4-yl)-2(S)-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)]-amide;

quinoxaline-2-carboxylic acid [1(S)-cyclohexylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-(4,4-difluoro-1-hydroxy-cyclohexyl)-2(S)-(hydroxy-4-hydroxycarbamoyl-butyl)]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4(S)-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-butyl]-amide;

quinoline-3-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiophen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-oct-6-enyl)]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)]-amide;

N-(1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-5,6-dichloro-nicotinamide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiazol-4-ylmethyl-octyl)-amide;

benzothiazole-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)]-amide; and

benzofuran-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)]-amide.

Examples of other compounds of the formula I are the following:

quinoxaline-2-carboxylic acid (4-carbamoyl-7-fluoro-2-hydroxy-7-methyl-1-thiazol-4-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid (7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-thiazol-4-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-1-thiazol-4-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-thiazol-4-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-thiazol-4-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-(4,4-difluoro-cyclohexyl)-2-hydroxy-4-hydroxycarbamoyl-1-thiazol-4-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-1-(3,5-difluoro-benzyl)-7-fluoro-2-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1-(3,5-difluoro-benzyl)-7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-1-(3,5-difluoro-benzyl)-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-1-(3,5-difluoro-benzyl)-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [1-(3,5-difluoro-benzyl)-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-4-hydroxycarbamoyl-butyl]-amide;

quinoxaline-2-carboxylic acid (4-carbamoyl-2-hydroxy-7-methyl-1-pyridin-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid (7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-pyridin-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(2,6-dimethyl-tetrahydro-pyran-4-yl)-2-hydroxy-1-pyridin-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-pyridin-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid (4-carbamoyl-4-cyclohexyl-2-hydroxy-1-pyridin-2-ylmethyl-butyl)-amide;

quinoxaline-2-carboxylic acid [4-(4,4-difluoro-cyclohexyl)-2-hydroxy-4-hydroxycarbamoyl-1-pyridin-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid (4-carbamoyl-7-fluoro-2-hydroxy-7-methyl-1-pyridin-3-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid (2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-pyridin-3-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-1-pyridin-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-(2,6-dimethyl-tetrahydro-pyran-4-yl)-2-hydroxy-4-hydroxycarbamoyl-1-pyridin-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-pyridin-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid (4-cyclohexyl-2-hydroxy-4-hydroxycarbamoyl-1-pyridin-3-ylmethyl-butyl)-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-7-fluoro-1-(4-fluoro-benzyl)-2-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [7-fluoro-1-(4-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-1-(4-fluoro-benzyl)-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1-(4-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-1-(4-fluoro-benzyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [4-(4,4-difluoro-cyclohexyl)-1-(4-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-1-(3-fluoro-benzyl)-2-hydroxy-4-(1-hydroxy-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [7-fluoro-1-(3-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(2,6-dimethyl-tetrahydro-pyran-4-yl)-1-(3-fluoro-benzyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [1-(3-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-1-(3-fluoro-benzyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [4-cyclohexyl-1-(3-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-1-(2-fluoro-benzyl)-2-hydroxy-4-(1-hydroxy-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [7-fluoro-1-(2-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(2,6-dimethyl-tetrahydro-pyran-4-yl)-1-(2-fluoro-benzyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [1-(2-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-1-(2-fluoro-benzyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [4-cyclohexyl-1-(2-fluoro-benzyl)-2-hydroxy-4-hydroxycarbamoyl-butyl]-amide;

quinoxaline-2-carboxylic acid (4-carbamoyl-7-fluoro-2-hydroxy-7-methyl-1-thiophen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid (7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-thiophen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-1-thiophen-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-thiophen-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-thiophen-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-(4,4-difluoro-cyclohexyl)-2-hydroxy-4-hydroxycarbamoyl-1-thiophen-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-2-hydroxy-7-methyl-1-(3-trifluoromethyl-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-(3-trifluoromethyl-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-carbamoyl-4-(4-hydroxy-2,6-dimethyl-tetrahydro-pyran-4-yl)-1-(3-trifluoromethyl-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-(3-trifluoromethyl-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid {4-carbamoyl-4-cyclohexyl)-2-hydroxy-1-(3-trifluoromethyl-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid {4-hydroxycarbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-(3-trifluoromethyl-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-carbamoyl-7-methyl-1-(3-trifluoromethoxy-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [4-hydroxycarbamoyl-2-hydroxy-7-methyl-1-(3-trifluoromethoxy-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-carbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-(3-trifluoromethoxy-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(4-hydroxy-2,6-dimethyl-tetrahydro-pyran-4-yl)-1-(3-trifluoromethoxy-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid {4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-(3-trifluoromethoxy-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid {4-hydroxycarbamoyl-4-cyclohexyl)-2-hydroxy-1-(3-trifluoromethoxy-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-carbamoyl-7-methyl-1-(4-trifluoromethoxy-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-(4-trifluoromethoxy-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-carbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-(4-trifluoromethoxy-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-(4-trifluoromethoxy-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid {4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-(4-trifluoromethoxy-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid {4-hydroxycarbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-(4-trifluoromethoxy-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-2-hydroxy-7-methyl-1-(2-trifluoromethyl-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-(2-trifluoromethoxy-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-carbamoyl-4-(4-hydroxy-2,6-dimethyl-tetrahydro-pyran-4-yl)-1-(2-trifluoromethoxy-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-(2-trifluoromethoxy-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid {4-carbamoyl-4-cyclohexyl)-2-hydroxy-1-(2-trifluoromethoxy-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid {4-hydroxycarbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-(2-trifluoromethoxy-benzyl)-butyl}-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-carbamoyl-7-methyl-1-[3-(1-hydroxy-1-methyl-ethyl)-benzyl]-octyl]-amide;

quinoxaline-2-carboxylic acid [4-hydroxycarbamoyl-2-hydroxy-7-methyl -1-[3-(1-hydroxy-1-methyl-ethyl)-benzyl]-octyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-carbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-[3-(1-hydroxy-1-methyl-ethyl)-benzyl]-butyl}-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(4-hydroxy-2,6-dimethyl-tetrahydro-pyran-4-yl)-1-3-(1-hydroxy-1-methyl-ethyl)-benzyl)-butyl]-amide;

quinoxaline-2-carboxylic acid {4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-[3-(1-hydroxy-1-methyl-ethyl)-benzyl]-butyl}-amide;

quinoxaline-2-carboxylic acid {4-hydroxycarbamoyl-4-(cyclohexyl)-2-hydroxy-1-[3-(1-hydroxy-1-methyl-ethyl)-benzyl]-butyl}-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-carbamoyl-7-methyl-1-thiophen-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-1-thiophen-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-carbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-thiophen-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-1-thiophen-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-thiophen-3-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [4-hydroxycarbamoyl-4-(4,4-difluoro-cyclohexyl)-2-hydroxy-1-thiophen-3-ylmethyl-butyl]-amide;

[[1,8]naphthyridine-3-carboxylic acid (1-benzyl-4-carbamoyl-7-fluoro-2-hydroxy-7-methyl-octyl)-amide;

[1,8]naphthyridine-3-carboxylic acid (1-benzyl-7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl)-amide;

[1,8]naphthyridine-3-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

[1,8]naphthyridine-3-carboxylic acid [1-benzyl-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

[1,5]naphthyridine-3-carboxylic acid (1-benzyl-4-carbamoyl-7-fluoro-2-hydroxy-7-methyl-octyl)-amide;

[1,5]naphthyridine-3-carboxylic acid (1-benzyl-7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl)-amide;

[1,5]naphthyridine-3-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

[1,5]naphthyridine-3-carboxylic acid [1-benzyl-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

[1,8]naphthyridine-2-carboxylic acid (1-benzyl-4-carbamoyl-7-fluoro-2-hydroxy-7-methyl-octyl)-amide;

[1,8]naphthyridine-2-carboxylic acid (1-benzyl-7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl)-amide;

[1,8]naphthyridine-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

[1,8]naphthyridine-2-carboxylic acid [1-benzyl-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

[1,6]naphthyridine-2-carboxylic acid (1-benzyl-4-carbamoyl-7-fluoro-2-hydroxy-7-methyl-octyl)-amide;

[1,6]naphthyridine-2-carboxylic acid (1-benzyl-7-fluoro-2-hydroxy-4-hydroxycarbamoyl-7-methyl-octyl)-amide;

[1,6]naphthyridine-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

[1,6]naphthyridine-2-carboxylic acid [1-benzyl-2-hydroxy-4-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid (6-chloro-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(S)-methylcarbamoyl-hept-6-enyl)-amide;

quinoline-3-carboxylic acid (2(S)-hydroxy-1(S)-isobutyl-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-sec-butyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-hept-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-hept-6-enyl)-amide;

N-1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-5-phenyl-nicotinamide;

quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-4(R)-dimethylcarbamoyl-2(S)-hydroxy-6-methyl-hept-6-enyl)-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

isoquinoline-4(R)-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid (4(R)-carbamoyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-heptyl)-amide;

quinoline-3-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-5-phenyl-pentyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-5-phenyl-pentyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-cyclobutylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-benzylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-cyclopropylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-ethylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-propylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid [1-benzyl-2(S)-hydroxy-4(R)-(2(S)-hydroxy-ethylcarbamoyl)-6-methyl-heptyl]-amide;

cinnoline-4(R)-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

isoquinoline-4(R)-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

N-1(S)-Benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-5-bromo-nicotinamide;

quinoline-3-carboxylic acid 1(R)-cyclohexylmethyl-2(R)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid [1-(4-benzyloxy-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

quinoline-3-carboxylic acid [1-(4-benzyloxy-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

isoquinoline-1-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-4(R)-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-6-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid [2(S)-hydroxy-1-(4-hydroxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

quinoline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

naphthalene-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclohex-1-enyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoline-3-carboxylic acid [1-benzyl-2(S)-hydroxy-6-methyl-4(R)-(3-methyl-butylcarbamoyl)-heptyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide;

trifluoro-methanesulfonic acid 4-{3(S)-hydroxy-7-methyl-5(R)-methylcarbamoyl-2(S)-[(quinoline-3-carbonyl)-amino]-octyl}-phenyl ester;

trifluoro-methanesulfonic acid 4-{3(S)-hydroxy-7-methyl-5(R)-methylcarbamoyl-2(S)-[(quinoxaline-2-carbonyl)-amino]-octyl}-phenyl ester;

quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

isoquinoline-3-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

N-1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-5-bromo-nicotinamide;

quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-prop-2-ynylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-hydroxycarbamoyl-6-methyl-heptyl)-amide;

quinoline-3-carboxylic acid 2(S)-hydroxy-1(S)-(4-methoxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

isoquinoline-3-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

5-bromo-N-(5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-nicotinamide;

quinoxaline-2-carboxylic acid [2(S)-hydroxy-1(S)-(4-methoxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

isoquinoline-4(R)-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoline-2-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

isoquinoline-4(R)-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoxaline-2-carboxylic acid [2(S)-hydroxy-1(S)-(4-hydroxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

quinoxaline-2-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoline-3-carboxylic acid [1(S)-(4-chloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(4-chloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoline-3-carboxylic acid [1(S)-(4-chloro-benzyl)-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(4-chloro-benzyl)-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide;

quinoline-2-carboxylic acid [1(S)-(4-chloro-benzyl)-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide;

benzofuran-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

N-1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-5,6-dichloro-nicotinamide;

quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

N-1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-5-bromo-nicotinamide;

5,6,7,8-tetrahydro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

isoquinoline-4(R)-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1-(3,4-dichloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

benzo[b]thiophene-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

2-methyl-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

6,7-dimethoxy-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

6,7-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

1H-benzoimidazole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

5-methyl-pyrazine-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoline-3-carboxylic acid [1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

5-chloro-1H-indole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

2-methoxy-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcabamoyl-heptyl)-amide;

5,6-dichloro-1H-benzoimidazole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

benzothiazole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

7,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

6,7,8-trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

5,8-dimethyl-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoline-3-carboxylic acid [1(S)-(3,4-dichloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

5,6,7,8-tetrahydro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

N-1(S)-benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-5-bromo-nicotinamide;

5,6,7,8-tetrahydro-quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-5-cyclopentyl-2(S)-hydroxy-pentyl)-amide;

6,7-dihydro-5H-[1]pyrindine-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-(4,4-difluoro-cyclohexylmethyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(4,4-difluoro-cyclohexylmethyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-ethylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-propylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-cyclopropylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-cyclobutylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-(4-difluoromethoxy-benzyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide;

4-{3(S)-hydroxy-7-methyl-5(R)-methylcarbamoyl-2(S)-[(quinoxaline-2-carbonyl)-amino]-octyl}-benzoic acid methyl ester;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-butyl)-amide;

6,7,8-trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

6,7,8-trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

6,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

6,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-5-cyclopentyl-2(S)-hydroxy-pentyl)-amide;

6-methyl-pyridine-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-8-methyl-4(R)-methylcarbamoyl-nonyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-8-methyl-nonyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-biphenyl-4(R)-ylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-oct-6-enyl)-amide;

quinoxaline-2-carboxylic acid (2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-1(S)-naphthalen-2-ylmethyl-heptyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7,7-dimethyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7,7-dimethyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-biphenyl-4(R)-ylmethyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-5-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(3-fluoro-benzyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3(S)-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-oct-6-enyl)-amide;

6,7,8-trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-nonyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-nonyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-nonyl)- amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-dimethylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

7,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-4(R)-methylcarbamoyl-5-phenyl-pentyl)-amide;

7,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

8-fluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-4(R)-methylcarbamoyl-non-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-non-6-enyl)-amide;

7,8 difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

8-fluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide;

4(S)hydroxy-2(R)-(3-methyl-butyl)-6-phenyl-5(S)-[(quinoxaline-2(R)-carbonyl)-amino]-hexanoic acid;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-nonyl)-amide;

2-{2(S)-hydroxy-4-phenyl-3(S)-[(quinoxaline-2-carbonyl)-amino]-butyl}-N1, N4-dimethyl-succinamide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4-ethylcarbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid [7-fluoro-1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3,4-dichloro-benzyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide;

7,8-difluoro-quinoline-3-carboxylic acid [4(R)-carbamoyl-1(S)-(3,4-dichloro-benzyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-phenethyl-octyl)-amide;

7,8-difluoro-quinoline-3-carboxylic acid [4(R)-carbamoyl-7-fluoro-1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid {1(S)-[4(R)-(3-methyl-butyl)-5-oxo-tetrahydro-furan-2-yl]-2(S)-phenyl-ethyl}-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(4-methyl-piperazine-1-carbonyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(tetrahydro-pyran-4(R)-yl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(piperidine-1-carbonyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(morpholine-4(R)-carbonyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(3-morpholin-4-yl-propionyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-3-(2-carbamoyl-indan-2-yl)-2(S)-hydroxy-propyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-4(R)-methylcarbamoyl-7-phenyl-hept-6-enyl)-amide;

quinoline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

6,7-dihydro-5H-[1]pyrindine-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclohexyl-2(S)-hydroxy-butyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclohexyl-2(S)-hydroxy-butyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclohexyl-2(S)-hydroxy-butyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclopentyl-2(S)-hydroxy-butyl)-amide;

quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

N-1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-5-bromo-nicotinamide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1-(2(S)-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(2(S)-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-4(S)-(4-isopropyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiophen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiazol-4(R)-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4(S)-(3,3,5,5-tetramethyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4(S)-indan-2-yl-butyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4(S)-cycloheptyl-2(S)-hydroxy-butyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-propyl-octyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-propyl-oct-5-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2,7-dihydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-7-chloro-2(S)-hydroxy-4(R)-methylcarbamoyl-hept-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-7-chloro-2(S)-hydroxy-4(R)-methylcarbamoyl-hept-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-6-chloro-2(S)-hydroxy-4(S)-methylcarbamoyl-hept-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-6-chloro-2(S)-hydroxy-hept-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-6-cyclopropyl-2(S)-hydroxy-hexyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-6-cyclopropyl-2(S)-hydroxy-4(R)-methylcarbamoyl-hexyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-4(S)-(4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-4(S)-indan-2-yl-butyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(4-trifluoromethoxy-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4(R)-carbamoyl-5-(4-fluoro-phenyl)-2(S)-hydroxy-pentyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-hept-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-hept-6-enyl)-amide;

3-Hydroxy-quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-benzylcarbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(pyridin-3-ylmethyl)-carbamoyl]-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-8,8-trifluoro-2(S)-hydroxy-4(R)-methylcarbamoyl-7-trifluoromethyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-8,8-trifluoro-2(S)-hydroxy-7-trifluoromethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-1(S)-(4-methylcarbamoyl-benzyl)-octyl]-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-5-ethyl-2(S)-hydroxy-heptyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4(S)-(tetrahydro-pyran-4-yl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2(R)-pyridin-2-yl-ethylcarbamoyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-(3,4-dimethoxy-benzylcarbamoyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-6-methoxy-hexyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-oct-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-7-chloro-2(S)-hydroxy-4(R)-methylcarbamoyl-oct-6-enyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-4(S)-(3,5-dimethyl-cyclohexyl)-2(S)-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(pyridin-2-ylmethyl)-carbamoyl]-octyl}-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-[2-(4-hydroxy-phenyl)-ethylcarbamoyl]-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(thiophen-2-ylmethyl)-carbamoyl]-octyl}-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-6-phenoxy-hexyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-6-isopropoxy-hexyl)-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[2-(4-sulfamoyl-phenyl)-ethylcarbamoyl]-octyl}-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(pyridin-4-ylmethyl)-carbamoyl]-octyl}-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4-(2-ethylsulfanyl-ethylcarbamoyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(2-methoxy-ethylcarbamoyl)-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2-pyridin-3-yl-ethylcarbamoyl)-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2-pyridin-4(R)-yl-ethylcarbamoyl)-octyl]-amide;

quinoxaline-6-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-6-tert-butoxy-4(R)-carbamoyl-2(S)-hydroxy-hexyl)-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[2-1(S)-methyl-1H-pyrrol-2-yl)-ethylcarbamoyl]-octyl}-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(1,1-dioxo-hexahydro-thiopyran-4-yl)-2(S)-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-[2-(6-methoxy-1H-indol-3-yl)-ethylcarbamoyl]-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(2-methoxy-benzylcarbamoyl)-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(3-methoxy-benzylcarbamoyl)-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2-thiophen-2-yl-ethylcarbamoyl)-octyl]-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-[2-(1H-indol-3-yl)-ethylcarbamoyl]-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid {4(R)-[2-(4-amino-phenyl)-ethylcarbamoyl]-1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-4(R)-[2-(3,5-dimethoxy-phenyl)-ethylcarbamoyl]-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-4(R)-[2-(3,4-dimethoxy-phenyl)-ethylcarbamoyl]-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-4(R)-[(furan-2-ylmethyl)-carbamoyl]-2(S)-hydroxy-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-4(R)-[2-(2,5-dimethoxy-phenyl)-ethylcarbamoyl]-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(4-methoxy-benzylcarbamoyl)-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-6-cyclohexyloxy-2(S)-hydroxy-hexyl)-amide;

quinoxaline-2-carboxylic acid {4(R)-[(1H-benzoimidazol-2-ylmethyl)-carbamoyl]-1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(2(S)-hydroxymethyl-pyrrolidine-1-carbonyl)-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(tetrahydrofuran-2-ylmethyl)-carbamoyl]-octyl}-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4-carbamoyl-4(S)-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-(2,3-dimethoxy-benzylcarbamoyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(2,6-dimethyl-tetrahydro-pyran-4-yl)-2(S)-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-1(S)-(3-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

7,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

N-1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-5,6-dichloro-nicotinamide;

benzofuran-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

cinnoline-4(R)-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-1-(4-iodo-benzyl)-7-methyl-octyl]-amide;

pyrazine-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

6,7,8-trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoline-6-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

isoquinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

2-methoxy-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

1H-benzoimidazole-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

benzothiazole-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

5-methyl-pyrazine-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-pyridin-3-yl-pentyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclohexyl)-butyl]-amide;

quinoline-3-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide;

quinoline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide;

fluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide;

N-(1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-5,6-dichloro-nicotinamide;

N-(1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-5-bromo-nicotinamide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-1-phenyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-pyridin-2-yl-pentyl)-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclohexyl)-1(S)-thiophen-2-ylmethyl-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(4-hydroxy-tetrahydro-thiopyran-4-yl)-butyl]-amide;

1,3-dimethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-methoxycarbamoyl-7-methyl-octyl)-amide;

7,8-difluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(2-chloro-phenyl)-2(S)-hydroxy-pentyl]-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-o-tolyl-pentyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-2(S)-hydroxy-4(R)-hydroxycarbamoyl-5-phenyl-pentyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclopentyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-5-(3,4-dichloro-phenyl)-2(S)-hydroxy-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(2-fluoro-phenyl)-2(S)-hydroxy-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-cyclopentyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-3-methyl-cyclopentyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

N-(1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-5-bromo-nicotinamide;

8-Fluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide;

6,7-dihydro-5H-[1]pyrindine-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide;

quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-3,5-dimethyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-3,5-dimethyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cycloheptyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-cycloheptyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(3-fluoro-phenyl)-2(S)-hydroxy-pentyl]-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-m-tolyl-pentyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-2(S)-hydroxy-4-isobutylcarbamoyl-butyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(2-hydroxy-adamantan-2-yl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(9-hydroxy-bicyclo[3.3.1]non-9-yl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-(2-hydroxy-adamantan-2-yl)-4-hydroxycarbamoyl-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-(9-hydroxy-bicyclo[3.3.1]non-9-yl)-4-hydroxycarbamoyl-buty l]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(3-methoxy-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4-propyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4-propyl-cyclohexyl)-butyl]- amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(4-methoxy-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4(S)-(4-ethyl-1-hydroxy-cyclohexyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4,4-dimethyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4,4-dimethyl-cyclohexyl)-but yl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(4,4-difluoro-1-hydroxy-cyclohexyl)-2-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3,5-difluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid 4(R)-carbamoyl-1(S)-(3-chloro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(3-chloro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide;

7,8-Difluoro-quinoline-3-carboxylic acid (1S)-benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide;

6,7,8-Trifluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-(3,5-difluoro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid (1(S)-benzyl-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl)-amide;

7,8-Difluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-ethylcarbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide;

N-(1(S)-Benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-4-trifluoromethyl-nicotinamide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(2-chloro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

7,8-Difluoro-quinoline-3-carboxylic acid [(4R)-carbamoyl-1(S)-(3-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(2-fluoro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-1(S)-thiophen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(2-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-(3,4-difluoro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3,4-difluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-1(S)-naphthalen-1-ylmethyl-octyl)-amide;

6,7,8-Trifluoro-quinoline-3-carboxylic acid [4(R)-carbamoyl-1(S)-(3-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-1(S)-naphthalen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid (2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-1(S)-naphthalen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid (1(S)-benzo[b]thiophen-3-ylmethyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(4-hydroxy-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(3-hydroxy-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(2-hydroxy-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(2-hydroxy-5-methyl-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(2-hydroxy-3-methyl-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-5-(3-ethoxy-2-hydroxy-phenyl)-2-hydroxy-pentyl]-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(4-hydroxy-3,5-dimethyl-phenyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid (1-benzyl-4-carbamoyl-2,6-dihydroxy-6-methyl-heptyl)-amide;

quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(1-hydroxy-cyclohexyl)-pentyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-(4,4-difluoro-1-hydroxy-cyclohexyl)-2(S)-hydroxy-4-hydroxycarbamoyl-but yl]-amide; and

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4-trifluoromethyl-cyclohexyl)-butyl]-amide.

The present invention also relates to a pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases (such as rheumatoid arthritis, type I diabetes (recent onset), inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis), acute and chronic inflammatory conditions (such as osteoarthritis, adult respiratory distress syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, and glomerulonephritis), allergic conditions (such as asthma and atopic dermatitis), infection associated with inflammation (such as viral inflammation (including influenza and hepatitis) and Guillian-Barre), transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases (including sarcoidosis, leprosy and tuberculosis). in a mammal, preferably a human, comprising an amount of a compound of the formula I or a pharmaceutically acceptable salt thereof effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

The present invention also relates to a pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by inhibiting MIP-1α binding to the receptor CCR1 in a mammal, preferably a human, comprising an amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier. Examples of such disorders and conditions are those enumerated in the preceding paragraph.

The present invention also relates to a method for treating or preventing a disorder or condition selected from autoimmune diseases (such as rheumatoid arthritis, type I diabetes (recent onset), inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis), acute and chronic inflammatory conditions (such as osteoarthritis, adult respiratory distress syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, and glomerulonephritis), allergic conditions (such as asthma and atopic dermatitis), infection associated with inflammation (such as viral inflammation (including influenza and hepatitis) and Guillian-Barre), transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases (including sarcoidosis, leprosy and tuberculosis) in a mammal, preferably a human, comprising administering to a mammal in need of such treatment or prevention an amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition.

The present invention also relates to a method for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal, preferably a human, comprising administering to a mammal in need of such treatment or

prevention an amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition.

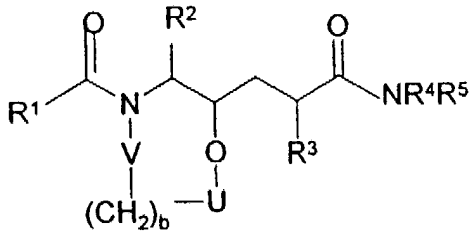
The present invention also relates to a pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases (such as rheumatoid arthritis, type I diabetes (recent onset), inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis), acute and chronic inflammatory conditions (such as osteoarthritis, adult respiratory distress syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, and glomerulonephritis), allergic conditions (such as asthma and atopic dermatitis), infection associated with inflammation (such as viral inflammation (including influenza and hepatitis) and Guillian-Barre), transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases (including sarcoidosis, leprosy and tuberculosis) in a mammal, preferably a human, comprising a CCR1 receptor antagonizing effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The present invention also relates to a pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal, preferably a human, comprising a CCR1 receptor antagonizing effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

The present invention also relates to a method for treating or preventing a disorder or condition selected from autoimmune diseases (such as rheumatoid arthritis, type I diabetes (recent onset), inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis), acute and chronic inflammatory conditions (such as osteoarthritis, adult respiratory distress syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, and glomerulonephritis), allergic conditions (such as asthma and atopic dermatitis), infection associated with inflammation (such as viral inflammation (including influenza and hepatitis) and Guillian-Barre), transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases (including sarcoidosis, leprosy and tuberculosis) in a mammal, preferably a human, comprising administering to a mammal in need of such treatment or prevention a CCR1 receptor antagonizing effective amount of a compound of formula I, or a pharmaceutically acceptable salt thereof.

This invention also encompasses pharmaceutical compositions containing and methods of treating or preventing comprising administering prodrugs of compounds of the

formula I. Compounds of formula I having free amino, amido, hydroxy or carboxylic groups can be converted into prodrugs. Prodrugs include compounds wherein an amino acid residue, or a polypeptide chain of two or more (e.g., two, three or four) amino acid residues which are covalently joined through peptide bonds to free amino, hydroxy or carboxylic acid groups of compounds of formula I. The amino acid residues include the 20 naturally occurring amino acids commonly designated by three letter symbols and also include, 4-hydroxyproline, hydroxylysine, demosine, isodemosine, 3-methylhistidine, norvalin, beta-alanine, gamma-aminobutyric acid, citrulline homocysteine, homoserine, ornithine and methionine sulfone. Prodrugs also include compounds wherein carbonates, carbamates, amides and alkyl esters which are covalently bonded to the above substituents of formula I through the carbonyl carbon prodrug sidechain. Prodrugs also include compounds of formula I in which the secondary amide and its ß-hydroxy when taken together form a group of the formula



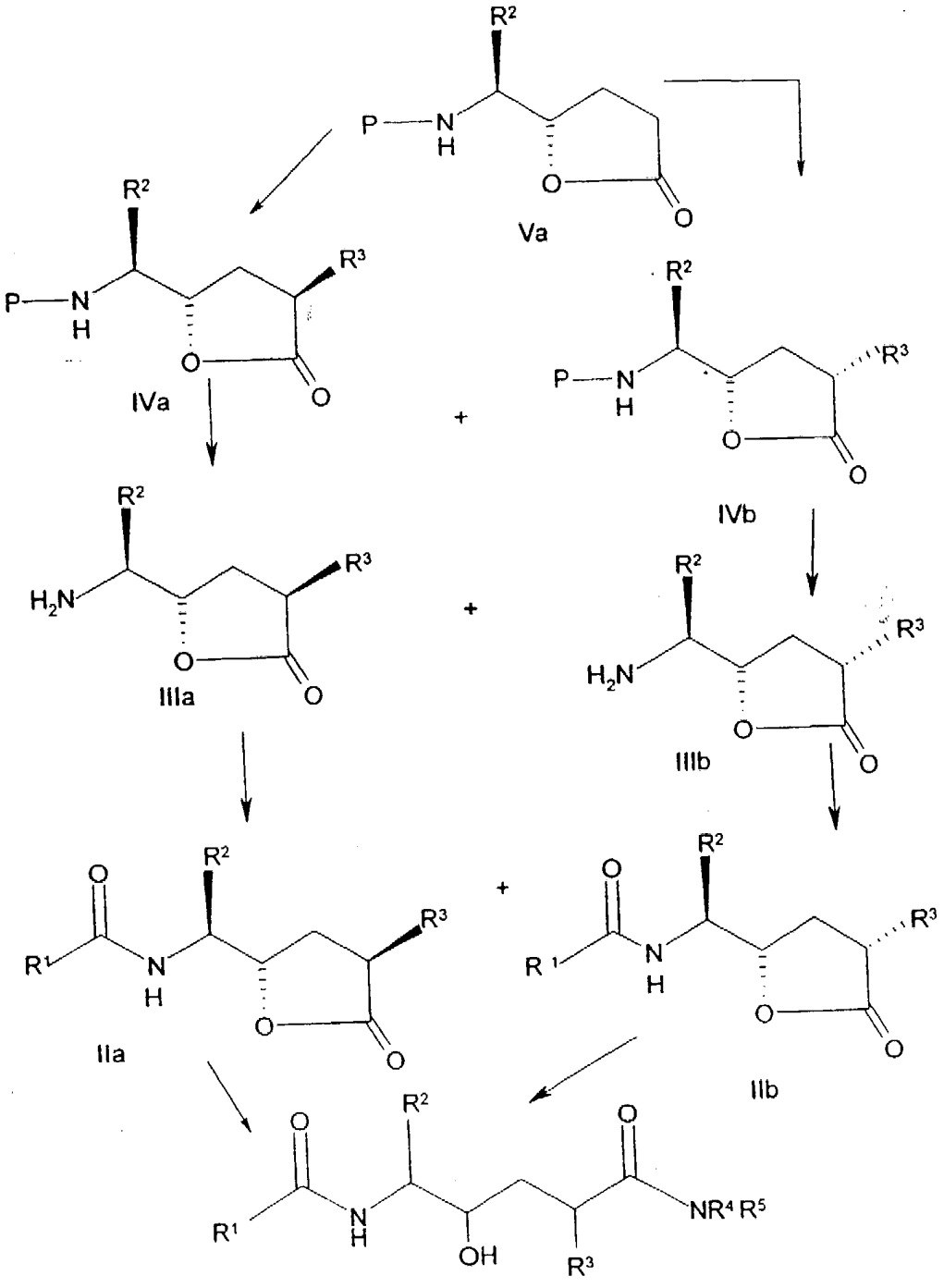
I'

wherein R^1, R^2 , R^3, R^4 and R^5 are as defined in formula I and U and V are independently carbonyl, methylene, SO_2 or SO_3, and b is an integer from one to three wherein each methylene group is optionally substituted with hydroxy.

Detailed Description of the Invention

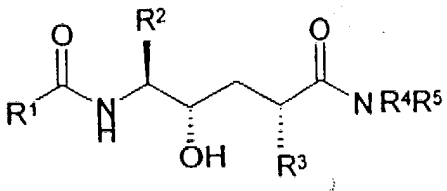
Compounds of the formula I may be prepared according to the following reaction schemes and discussion. Unless otherwise indicated g, n, m, p, and R^1 through R^6 and structural formula I in the reaction Schemes and discussion that follow are as defined above.

SCHEME 1



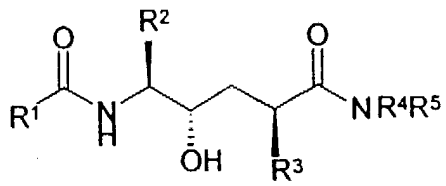
I

Scheme 1 refers to the preparation of compounds of the formula I having the exact stereochemistry



Ia

or



Ib

Compounds of the formula Ia and Ib, or any of the intermediates thereof, can be separated by column chromatography according to methods well known to those of ordinary skill in the art, to yield pure compounds of the formula Ia and Ib.

Referring to Scheme 1, compounds of the formula I, wherein either or both R^4 or R^5 are other than hydrogen, are prepared from compounds of the formula II (i.e. IIa and IIb) by reaction with a compound of the formula R^4R^5NH in a polar solvent at a temperature from about 0°C to about 100°C, preferably the boiling point of the solvent used, i.e. 65°C when methanol is the solvent. Suitable solvents include, alcohols, such as methanol, ethanol, or butanols or ethers such as glyme or dioxane (an acid catalyst is preferably used with an ether solvent). Preferably the solvent is dioxane.

Alternatively, compounds of formula I, wherein either or both R^4 and R^5 are hydrogen, can be prepared from compounds of formula II, (i.e. IIa and IIb) by reaction with ammonia or another volatile amine in a polar solvent at a temperature from about -10°C to about 35°C, preferably at about 30°C. Suitable solvents include, alcohols, such as methanol, ethanol, or butanols; or ethers such as glyme or dioxane (an acid catalyst may be used with an ether solvent). Preferably the solvent is methanol.

Compounds of formula II are prepared by coupling a compound of formula III (i.e. IIIa and IIIb) with an acid of the formula R^1CO_2H. Such a coupling reaction is generally conducted at a temperature of about -30°C to about 80°C, preferably about 0°C to about 25°C. Examples of suitable coupling reagents which activate the carboxylic acid functionality are dicyclohexylcarbodiimide/hydroxybenzotriazole (DCC/HBT), N-3-dimethylaminopropyl-N'-ethylcarbodiimide (EDC)/HBT, 2-ethyoxy-1-ethoxycarbonyl-1,2-dihydroquinoline (EEDQ), carbonyl diimidazole (CDI)/dimethylaminopyridine (DMAP), and diethylphosphorylcyanide. The coupling is conducted in an inert solvent, preferably an

aprotic solvent, such as acetonitirile, dichloromethane, chloroform, and dimethylformamide. The preferred solvent is dichloromethane.

For a discussion of other conditions used for amide coupling see Houben-Weyl, Vol. XV, part II, E. Wunsch, Ed., George Theime Veriag, 1974, Stuttgart, and those described in M. Bodanszky. Principles of Peptide Synthesis, Springer-Verlag, Berlin (1984) and The Peptides, Analysis, Synthesis and Biology (ed. E. Gross and J. Meienhofer), Vois 1-5. (Academic Press, New York) 1979-1983.

The compounds of formula III, wherein R^3 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl-$(CH_2)_n$-, $(C_2\text{-}C_9)$heterocycloalkyl-$(CH_2)_n$-, $(C_2\text{-}C_9)$heteroaryl-$(CH_2)_n$-, or aryl-$(CH_2)_n$- can be prepared by deprotection of compounds of the formula IV (i.e. IVa and IVb). Suitable protecting groups, of the formula P, include carbobenzyloxy, t-butoxy carbonyl or 9-fluorenyl-methylenoxy carbonyl.

For example:

(a) If the protecting group, P, of the compound of the formula IV is carbobenzyloxy, the latter may be removed by hydrogenation with a nobel metal catalyst such as palladium or palladium hydroxide on carbon in the presence of hydrogen. The hydrogenation is generally conducted at a temperature of about 0°C to about 100°C, preferably about 20°C to 50°C.

(b) If the protecting group, P, is t-butoxycarbonyl group, such group may be removed by acidolysis. Acidolysis may be conducted with HCl in dioxane or with trifluoracetic acid in methylene chloride at a temperature of about -30°C to about -70°C, preferably about -5°C to about 35°C.

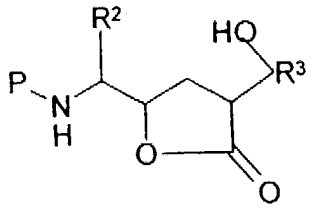
(c) If the protecting group, P, is 9-fluorenylmethylenoxycarbonyl, such group may be removed by treatment with an amine base, preferably piperidine. This reaction may be run in piperidine as solvent at 10°C to about 100°C, preferably at 25°C.

Compounds of the formula III, wherein R^3 is substituted $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl-$(CH_2)_n$- or $(C_2\text{-}C_9)$heterocycloalkyl-$(CH_2)_n$- may be prepared from compounds of the formula IV, wherein R^3 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl-$(CH_2)_n$- or $(C_2\text{-}C_9)$heterocycloalkyl-$(CH_2)_n$-, wherein one of the carbon-carbon single bonds is replaced by a carbon-carbon double bond, by methods well known to those of ordinary skill in the art. Specifically, one example of introduction of substitution into the R^3 group, a compound of formula III, wherein R^3 is $(C_1\text{-}C_{10})$alkyl substituted by one to three fluoro groups can be prepared from compounds of the formula IV, wherein R^3 is $(C_1\text{-}C_{10})$alkyl, wherein one of the carbon-carbon single bonds of said $(C_1\text{-}C_{10})$alkyl has been replaced by a carbon-carbon double bond, by reaction with hydrogen fluoride in pyridine (i.e. pyridinium poly(hydrogen

fluoride), in a reaction inert solvent. Suitable solvents include cyclohexane, toluene or benzene, preferably benzene. The aforesaid reaction is run at a temperature from about -78°C to about 35°C. Preferably, this reaction is carried out in benzene at about 25°C.

Compounds of the formula IV , wherein R^3 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl-$(CH_2)_n$-, $(C_2\text{-}C_9)$heterocycloalkyl-$(CH_2)_n$-, $(C_2\text{-}C_9)$heteroaryl-$(CH_2)_n$- or aryl-$(CH_2)_n$-, wherein n is other than zero, can be prepared by reaction of a compound of formula V with a compound of the formula R^3-L, wherein L is a leaving group, in the presence of a strong base in an aprotic polar solvent. Suitable leaving groups include chloro, fluoro, bromo, iodo, mesylate, triflate or tosylate. Preferably, the leaving group is a triflate, iodide or bromide. Triflates may be easily prepared according to the method of Beard, et al., J Org Chem., 38. 3673 (1973). Suitable bases include lithium dialkyl amides such as lithium N-isopropyl-N-cyclohexylamide or potassium hydride. Suitable solvents include ethers (such as THF, glyme or dioxane) benzene or toluene, preferably THF. The aforesaid reaction is conducted at about -78°C to about 0°C, preferably at about -78°C.

Alternatively, compounds of the formula IV, wherein R^3 is $(C_1\text{-}C_{10})$alkyl, $(C_3\text{-}C_{10})$cycloalkyl-$(CH_2)_n$- or $(C_2\text{-}C_9)$heterocycloalkyl-$(CH_2)_n$- can be prepared by reaction of a compound of formula V with an aldehyde or ketone precursor of R^3 in an aldol condensation. For example, a compound of the formula V can be reacted with a compound of the formula R^3(=O) in the presence of a base, to form an aldol intermediate of the formula



VI

which may be isolated and taken on to final product or converted directly in the same reaction step to a compound of the formula IV by the loss of water. The degree of completion for the conversion of compounds of the formula II to the aldol product of formula I may be assessed using one or more analytical techniques, such as thin layer chromatography (tlc) or mass spectrometry. In some instances it may be possible or desirable to isolate the intermediate of formula VI. In such case, the compound of formula VI may be converted into the compound of formula IV by the elimination of water using techniques which are familiar to those skilled in the art, for example, by heating to the reflux temperature a solution of the compound of formula VI

in a solvent such as benzene, toluene or xylene, in the presence of a catalytic amount of phosphorous pentoxide, benzene- or p-toluene-sulfonic acid with provision for the removal of the water generated, preferably (methoxycarbonylsulfamoyl)-triethylammonium hydroxide (Burgess reagent). Such water removal techniques may involve the use of molecular sieves or a Dean-Stark trap to isolate the water created as an azeotrope with the solvent.

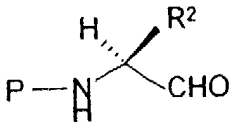
The aldol reaction is typically carried out in a polar solvent such as DMSO, DMF, tetrahydrofuran (THF), methanol or ethanol, at a temperature from about -78°C to about 80°C. Preferably, this reaction is carried out in THF at about -78°C. Suitable bases for use in the aldol formation step include potassium carbonate (K_2CO_3), sodium carbonate (Na_2CO_3), sodium hydride (NaH), sodium methoxide, potassium-tert.-butoxide, lithium diisopropylamide, pyrrolidine and piperidine. Lithium diisopropylamide is preferred. Aldol condensations are described in "Modern Synthetic Reactions," Herbert O. House, 2d. Edition, W.A. Benjamin, Menlo Park, California, 629-682 (1972), J. Org. Chem., 49, 2455 (1984), and Tetrahedron, 38 (20), 3059 (1982).

Compounds of the formula IV wherein R^3 is unsaturated can be converted to saturated analogues by hydrogenating the compounds containing a carbon-carbon double bond, using standard techniques that are well known to those skilled in the art. For example, reduction of the double bond may be effected with hydrogen gas (H_2), using catalysts such as palladium on carbon (Pd/C), palladium on barium sulfate ($Pd/BaSO_4$), platinum on carbon (Pt/C), or tris(triphenylphosphine) rhodium chloride (Wilkinson's catalyst), in an appropriate solvent such as methanol, ethanol, THF, dioxane or ethyl acetate, at a pressure from about 1 to about 5 atmospheres and a temperature from about 10°C to about 60°C, as described in Catalytic Hydrogenation in Organic Synthesis, Paul Rylander, Academic Press Inc., San Diego, 31-63 (1979). The following conditions are preferred: Pd on carbon, methanol at 25°C and 50 psi of hydrogen gas pressure. This method also provides for introduction of hydrogen isotopes (i.e., deuterium, tritium) by replacing $^1H_2$ with $^2H_2$ or $^3H_2$ in the above procedure.

An alternative procedure employing the use of reagents such as ammonium formate and Pd/C in methanol at the reflux temperature under an inert atmosphere (e.g., nitrogen or argon gas) is also effective in reducing the carbon-carbon double bond of compounds of the formula I. Another alternative method involves selective reduction of the carbon-carbon bond. This can be accomplished using samarium and iodine or samarium iodide (SmI_2) in methanol or ethanol at about room temperature, as described by R. Yanada et. al., Synlett., 443-4 (1995).

Compounds of the formula V can be prepared by methods well known to those of ordinary skill in the art or are commercially available. Specifically, compounds of the formula

Va and Vb (shown below) can be prepared by the method of Fray et al., (J. Org. Chem., 51, 4828-4833 (1986)) using an (S)-aldehyde of the formula

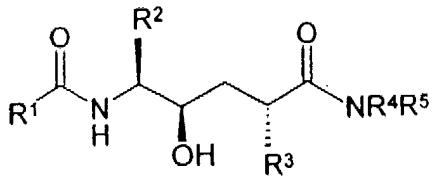


VII

Compounds of the formula VII are prepared by reducing amino acids or amino esters to alcohols (Stanfield et al., J. Org. Chem. 46, 4799-4800 (1981), Soai et al., Bull. Chem. Soc. Jpn., 57, 2327 (1984)) followed by oxidation of the alcohols to aldehydes of the formula VII (Luly et al., J.Org. Chem., 53 (26), 6109-6112 (1988) and Denis et al., J Org. Chem., 56 (24), 6939-6942 (1991).). Un-natural amino acids can be prepared according to the method of Myers et al., Tet. Lett. 36, (1995) and Myers et al. J. Am. Chem. Soc., 117, 8488-8489 (1995).

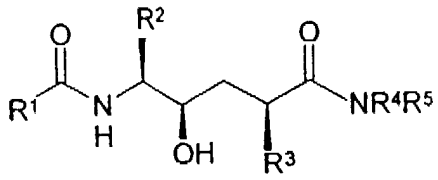
Alternatively, compounds of the formula V can also be made by the method of DeCamp et al., (Tetrahedron Lett., 32, 1867 (1991)).

Compounds of the formula I, with the exact stereochemistry

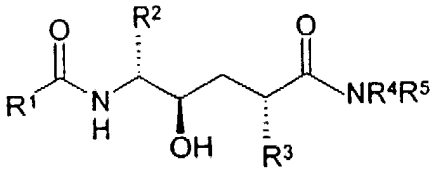


Ic

or

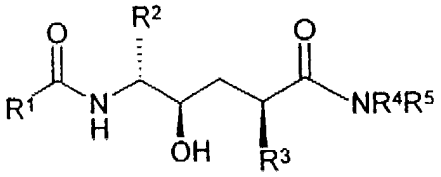


Id

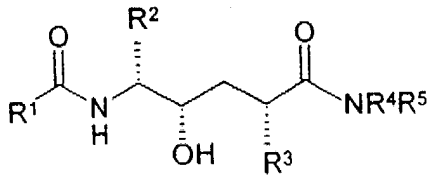


Ie

or

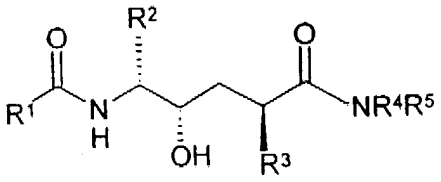


If



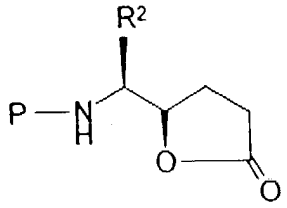
Ig

or



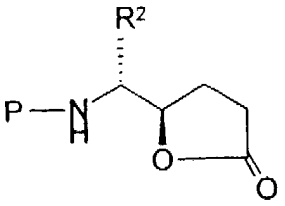
Ih

can be prepared according to the methods of Scheme 1, using either the minor lactone diastereomer of the formula,

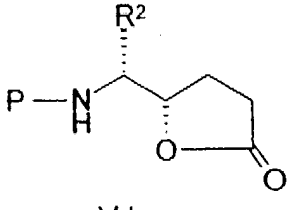


Vb

which can be prepared by the method of Fray, supra, from the (S)-aldehyde, or the alternate diastereomeric pair of the formula



Vc



Vd

which can be prepared using the corresponding (R)-aldehyde according to the method of Fray, supra.

Aldehyde or ketone precursors of the group R^3 are commercially available (e.g., cyclohexanone) or can be made by methods well known to those of ordinary skill in the art, such as described in J. Am. Chem. Soc., 90, 7001 (1968) and J. Org. Chem., 40, 574 (1975).

Unless indicated otherwise, the pressure of each of the above reactions is not critical. Generally, the reactions will be conducted at a pressure of about one to about three atmospheres, preferably at ambient pressure (about one atmosphere).

The compounds of the formula I which are basic in nature are capable of forming a wide variety of different salts with various inorganic and organic acids. Although such salts must be pharmaceutically acceptable for administration to animals, it is often desirable in practice to initially isolate a compound of the formula I from the reaction mixture as a pharmaceutically unacceptable salt and then simply convert the latter back to the free base compound by treatment with an alkaline reagent, and subsequently convert the free base to a pharmaceutically acceptable acid addition salt. The acid addition salts of the base compounds of this invention are readily prepared by treating the base compound with a substantially equivalent amount of the chosen mineral or organic acid in an aqueous solvent medium or in a suitable organic solvent such as methanol or ethanol. Upon careful evaporation of the solvent, the desired solid salt is obtained.

The acids which are used to prepare the pharmaceutically acceptable acid addition salts of the base compounds of this invention are those which form non-toxic acid addition salts, i.e., salts containing pharmacologically acceptable anions, such as hydrochloride, hydrobromide, hydroiodide, nitrate, sulfate or bisulfate, phosphate or acid phosphate, acetate, lactate, citrate or acid citrate, tartrate or bitartrate, succinate, maleate, fumarate, gluconate, saccharate, benzoate, methanesulfonate and pamoate [i.e., 1,1'-methylene-bis-(2-hydroxy-3-naphthoate)] salts.

Those compounds of the formula I which are also acidic in nature, are capable of forming base salts with various pharmacologically acceptable cations. Examples of such salts include the alkali metal or alkaline-earth metal salts and particularly, the sodium and

potassium salts. These salts are all prepared by conventional techniques. The chemical bases which are used as reagents to prepare the pharmaceutically acceptable base salts of this invention are those which form non-toxic base salts with the herein described acidic compounds of formula I. These non-toxic base salts include those derived from such pharmacologically acceptable cations as sodium, potassium, calcium and magnesium, etc. These salts can easily be prepared by treating the corresponding acidic compounds with an aqueous solution containing the desired pharmacologically acceptable cations, and then evaporating the resulting solution to dryness, preferably under reduced pressure. Alternatively, they may also be prepared by mixing lower alkanolic solutions of the acidic compounds and the desired alkali metal alkoxide together, and then evaporating the resulting solution to dryness in the same manner as before. In either case, stoichiometric quantities of reagents are preferably employed in order to ensure completeness of reaction and maximum product yields.

Compounds of the formula I and their pharmaceutically acceptable salts (hereinafter also referred to, collectively, as "the active compounds") are potent antagonists of the CCR1 receptors. The active compounds are useful in the treatment or prevention of autoimmune diseases (such as rheumatoid arthritis, type I diabetes (recent onset), inflammatory bowel disease, optic neuritis, psoriasis, multiple sclerosis, polymyalgia rheumatica, uveitis, and vasculitis), acute and chronic inflammatory conditions (such as osteoarthritis, adult respiratory distress syndrome, Respiratory Distress Syndrome of infancy, ischemia reperfusion injury, and glomerulonephritis), allergic conditions (such as asthma and atopic dermatitis), infection associated with inflammation (such as viral inflammation (including influenza and hepatitis) and Guillian-Barre), transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity (co-receptor usage), and granulomatous diseases (including sarcoidosis, leprosy and tuberculosis).

The activity of the compounds of the invention can be assessed according to procedures know to those of ordinary skill in the art. Examples of recognized methods for determining CCR1 induced migration can be found in Coligan, J. E., Kruisbeek, A.M., Margulies, D.H., Shevach, E.M., Strober, W. editors: Current Protocols In Immunology, 6.12.1- 6.12.3. (John Wiley and Sons, NY, 1991). One specific example of how to determine the activity of a compound for inhibiting migration is described in detail below.

Chemotaxis Assay:

The ability of compounds to inhibit the chemotaxis to various chemokines can be evaluated using standard 48 or 96 well Boyden Chambers with a 5 micron polycarbonate filter. All reagents and cells can be prepared in standard RPMI (BioWhitikker Inc.) tissue

culture medium supplemented with 1 mg/ml of bovine serum albumin. Briefly, MIP-1α (Peprotech, Inc., P.O. Box 275, Rocky Hill NJ) or other test agonists, were placed into the lower chambers of the Boyden chamber. A polycarbonate filter was then applied and the upper chamber fastened. The amount of agonist chosen is that determined to give the maximal amount of chemotaxis in this system (e.g., 1 nM for MIP-1α should be adequate).

THP-1 cells (ATCC TIB-202), primary human monocytes, or primary lymphocytes, isolated by standard techniques can then be added to the upper chambers in triplicate together with various concentrations of the test compound. Compound dilutions can be prepared using standard serological techniques and are mixed with cells prior to adding to the chamber.

After a suitable incubation period at 37 degrees centigrade (e.g. 3.5 hours for THP-1 cells, 90 minutes for primary monocytes), the chamber is removed, the cells in the upper chamber aspirated, the upper part of the filter wiped and the number of cells migrating can be determined according to the following method.

For THP-1 cells, the chamber (a 96 well variety manufactured by Neuroprobe) can be centrifuged to push cells off the lower chamber and the number of cells can be quantitated against a standard curve by a color change of the dye fluorocein diacetate.

For primary human monocytes, or lymphocytes, the filter can be stained with Dif Quik® dye (American Scientific Products) and the number of cells migrating can be determined microscopically.

The number of cells migrating in the presence of the compound are divided by the number of cells migrating in control wells (without the compound). The quotant is the % inhibition for the compound which can then be plotted using standard graphics techniques against the concentration of compound used. The 50% inhibition point is then determined using a line fit analysis for all concentrations tested. The line fit for all data points must have an coefficient of correlation (R squared) of > 90% to be considered a valid assay.

All of the compounds of the invention that were tested had IC_{50} of less than 25μM. in the Chemotaxis assay.

The compositions of the present invention may be formulated in a conventional manner using one or more pharmaceutically acceptable carriers. Thus, the active compounds of the invention may be formulated for oral, buccal, intranasal, parenteral (e.g., intravenous, intramuscular or subcutaneous) or rectal administration or in a form suitable for administration by inhalation or insufflation. The active compounds of the invention may also be formulated for sustained delivery.

For oral administration, the pharmaceutical compositions may take the form of, for example, tablets or capsules prepared by conventional means with pharmaceutically acceptable excipients such as binding agents (e.g., pregelatinized maize starch, polyvinylpyrrolidone or hydroxypropyl methylcellulose); fillers (e.g., lactose, microcrystalline cellulose or calcium phosphate); lubricants (e.g., magnesium stearate, talc or silica); disintegrants (e.g., potato starch or sodium starch glycolate); or wetting agents (e.g., sodium lauryl sulphate). The tablets may be coated by methods well known in the art. Liquid preparations for oral administration may take the form of, for example, solutions, syrups or suspensions, or they may be presented as a dry product for constitution with water or other suitable vehicle before use. Such liquid preparations may be prepared by conventional means with pharmaceutically acceptable additives such as suspending agents (e.g., sorbitol syrup, methyl cellulose or hydrogenated edible fats); emulsifying agents (e.g., lecithin or acacia); non-aqueous vehicles (e.g., almond oil, oily esters or ethyl alcohol); and preservatives (e.g., methyl or propyl p-hydroxybenzoates or sorbic acid).

For buccal administration, the composition may take the form of tablets or lozenges formulated in conventional manner.

The active compounds of the invention may be formulated for parenteral administration by injection, including using conventional catheterization techniques or infusion. Formulations for injection may be presented in unit dosage form, e.g., in ampules or in multi-dose containers, with an added preservative. The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles, and may contain formulating agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in powder form for reconstitution with a suitable vehicle, e.g., sterile pyrogen-free water, before use.

The active compounds of the invention may also be formulated in rectal compositions such as suppositories or retention enemas, e.g., containing conventional suppository bases such as cocoa butter or other glycerides.

For intranasal administration or administration by inhalation, the active compounds of the invention are conveniently delivered in the form of a solution or suspension from a pump spray container that is squeezed or pumped by the patient or as an aerosol spray presentation from a pressurized container or a nebulizer, with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas. In the case of a pressurized aerosol, the dosage unit may be determined by providing a valve to deliver a metered amount. The pressurized container or nebulizer may contain a solution or suspension of the active compound.

Capsules and cartridges (made, for example, from gelatin) for use in an inhaler or insufflator may be formulated containing a powder mix of a compound of the invention and a suitable powder base such as lactose or starch.

A proposed dose of the active compounds of the invention for oral, parenteral or buccal administration to the average adult human for the treatment of the conditions referred to above (e.g., rheumatoid arthritis) is 0.1 to 1000 mg of the active ingredient per unit dose which could be administered, for example, 1 to 4 times per day.

Aerosol formulations for treatment of the conditions referred to above (e.g., rheumatoid arthritis) in the average adult human are preferably arranged so that each metered dose or "puff" of aerosol contains 20 μg to 1000 μg of the compound of the invention. The overall daily dose with an aerosol will be within the range 0.1 mg to 1000 mg. Administration may be several times daily, for example 2, 3, 4 or 8 times, giving for example, 1, 2 or 3 doses each time.

The active agents can be formulated for sustained delivery according to methods well known to those of ordinary skill in the art. Examples of such formulations can be found in United States Patents 3,538,214, 4,060,598, 4,173,626, 3,119,742, and 3,492,397.

The compounds of the invention can also be utilized in combination therapy with other therapeutic agents such as with immunosuppressant agents such as cyclosporin A and FK-506, Cellcept®, rapamycin, leuflonamide or with classical anti-inflammatory agents (e.g. cyclooxygenase/lipoxegenase inhibitors) such as tenidap, aspirin, acetaminophen, naproxen and piroxicam, steroids including prednisone, azathioprine and biological agents such as OKT-3, anti IL-2 monoclonal antibodies (such as TAC),.

The following Examples illustrate the preparation of the compounds of the present invention. Melting points are uncorrected. NMR data are reported in parts per million (δ) and are referenced to the deuterium lock signal from the sample solvent (deuteriochloroform unless otherwise specified). Commercial reagents were utilized without further purification. THF refers to tetrahydrofuran. DMF refers to N,N-dimethylformamide. Chromatography refers to column chromatography performed using 32-63 mm silica gel and executed under nitrogen pressure (flash chromatography) conditions. Low Resolution Mass Spectra (LRMS) were recorded on either a Hewlett Packard 5989®, utilizing chemical ionization (ammonium), or a Fisons (or Micro Mass) Atmospheric Pressure Chemical Ionization (APCI) platform which uses a 50/50 mixture of acetonitrile/water with 0.1% formic acid as the ionizing agent. Room or ambient temperature refers to 20-25°C. All non-aqueous reactions were run under a nitrogen atmosphere for convenience and to maximize yields. Concentration at reduced pressure means that a rotary evaporator was used. The names

for the compounds of the invention were created by the Autonom 2.0 PC-batch version from Beilstein Informationssysteme GmbH (ISBN 3-89536-976-4).

EXAMPLE 1

QUINOLINE-3-CARBOXYLIC ACID (1(S)-CYCLOHEXYLMETHYL-2(S)-HYDROXY-6-METHYL-4(R)-METHYLCARBAMOYL-HEPTYL-6-ENYL)-AMIDE

METHOD A

QUINOLINE-3-CARBOXYLIC ACID {1-[4-(2-METHYLPROPEN-2-YL)-5-OXO-TETRAHYDROFURAN-2-YL]-2-CYCLOHEXYL-ETHYL}-AMIDE

To a solution of 1-{4-(2-methylpropen-2-yl)-[5-oxo-tetrahydrofuran-2-yl]-2-cyclohexyl-ethyl}-carbamic acid tert-butyl ester (302 mg, 0.83 mmol)(prepared according to the method of Fray, supra, except that (S)-2-(tert-butoxycarbonylamino)-3-cyclohexyl-1-propionaldehyde is the starting material aldehyde) in 15 mL of methylene chloride was added 1.5 mL of trifluoroacetic acid. The mixture was stirred at room temperature under a nitrogen atmosphere for 2 hours at which time the solvent was removed by azeotropic distillation under reduced pressure, using toluene as a cosolvent during the distillation. The resulting crude oil was dissolved in methylene chloride (5 mL) and quinoline-3-carboxylic acid (219 mg, 1.26 mmol), hydroxybenzotriazole (HOBT)(188 mg, 1.39 mmol), triethylamine (0.25 mL, 1.80 mmol) and N-3-dimethylaminopropyl-N'-ethylcarbodiimide (EDC)(248 mg, 1.29 mmol) was added. The resulting mixture was stirred at room temperature for 16 hours. The solution was transferred to a separatory funnel with 15 mL of methylene chloride and washed with 10% citric acid, saturated sodium bicarbonate and brine. The organic layer was dried over sodium sulfate and the solvent removed *in vacuo*. The remaining crude oil was purified by silica gel chromatography eluting with 3:1 hexanes: ethyl acetate to provide quinoline-3-carboxylic acid {1(S)-[4(R)-(2-methylpropen-2-yl)-5-oxo-tetrahydrofuran-2(S)-yl]-2-cyclohexyl-ethyl}-amide as a white foam (236 mg, 67%).

LRMS: 421 (MH+); ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90-1.89 (m, 13H), 1.63 (s, 3H), 2.03-2.14 (m, 2H), 2.38 (m, 2H), 2.48 (d, 1H, *J*=14.6 Hz), 2.73 (m, 1H), 4.63 (m, 2H), 4.69 (s, 1H), 4.79 (s, 1H), 6.9 (brs, 1H), 7.59 (t, 1H, *J*=7.8 Hz), 7.77 (t, 1H, *J*=8.4 Hz), 7.88 (d, 1H, *J*=8.3 Hz), 8.08 (d, 1H, *J*=8.4 Hz), 8.67 (s, 1H), 9.37 (d, 1H, *J*=2.1 Hz).

METHOD B

QUINOLINE-3-CARBOXYLIC ACID (1(S)-CYCLOHEXYLMETHYL-2(S)-HYDROXY-6-METHYL-4(R)-METHYLCARBAMOYL-HEPTYL-6-ENYL)-AMIDE

Methylamine was bubbled into a solution of the product from Method A (55 mg, 0.129 mmol) in methanol (2.5 mL). The solution was stirred for 2 hours at room temperature

and the solvent was removed under reduced pressure to provide the title compound (57 mg, 98%) as a pure white solid.

LRMS: 453 (MH+), 421, 283, 173; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.82-1.87 (m, 13H), 1.65 (s, 3H), 2.13 (dd, 1H, J=14.1, 8.7 Hz), 2.38 (d, 1H, J=14.2 Hz), 2.71 (d, 3H, J=4.7 Hz), 2.74 (m, 1H), 3.77 (d, 1H, J=8.7), 4.23 (br, 1H), 4.69 (s, 1H), 4.72 (s, 1H), 5.03 (brs, 1H), 6.60 (q, 1H, J=4.7Hz), 7.24 (d, 1H, J=9.3), 7.54 (t, 1H, J=7.1), 7.73 (t, 1H, J=7.1Hz), 7.81 (d, 1H, J=7.1 Hz), 8.04 (d, 1H, J=8.4), 8.61 (d, 1H, J=1.9), 9.33 (s, 1H).

EXAMPLE 2

QUINOXALINE-2-CARBOXYLIC ACID (1(S)-BENZYL-4(R)-BENZYLCARBAMOYL-7-FLUORO-2(S)-HYDROXY-7-METHYL-OCTYL)-AMIDE

ALLYLIC ALKYLATION

METHOD C:

{1(S)-[4(R)-(3-METHYL-BUT-2-ENYL)-5-OXO-TETRAHYDRO-FURAN-2(S)-YL]-2-PHENYL-ETHYL}-CARBAMIC ACID TERT-BUTYL ESTER

To a flame dried round bottom flask under a nitrogen atmosphere was added tetrahydrofuran (40 mL) followed by 1,1,1,3,3,3-hexamethyldisilazane (8 mL, 37.8 mmol). The mixture was cooled to 0°C and n-butyl lithium (14.5 mL of a 2.5 M solution in hexanes, 36.0 mmol) was added. The mixture was stirred for 15 minutes, then cooled to -78 °C in dry ice / acetone bath. {1(S)-[5-Oxo-tetrahydro-furan-2(S)-yl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester (5 g, 16.4 mmol) (prepared by the method of Fray, J. Org. Chem., (51) 4828 (1986)) dissolved in tetrahydrofuran (50 mL) was added dropwise via syringe and stirring continued for 30 minutes. A solution of 4-bromo-2-methyl-2-butene (2.07 mL, 18.0 mmol) in 40 mL of THF was added dropwise via syringe. Stirring was continued for 3 hours during which time the temperature rose to -60°C. The mixture was quenched by slow addition of saturated, aqueous ammonium chloride (25 mL). Upon warming to room temperature, the solution was diluted with ether (300 mL) and transferred to a separatory funnel. The organic phase was washed with saturated aqueous citric acid (2x100mL) , saturated aqueous sodium bicarbonate ($NaHCO_3$)(2x100mL), and 100 mL brine. The organic layer was dried over magnesium sulfate ($MgSO_4$) and the solvent removed under reduced pressure. Thin layer chromatography in 1:2 hexane/diethyl ether (Et_2O) revealed product with an R_f of 0.8. The resulting crude oil was chromatographed on silica gel (225g) eluting with 2:1 hexanes/diethyl ether to provide 4.73 g (77%) of the title compound. TLC: 1:2 Hexanes/Et_2O R_f: 0.8. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 ppm (5H, m), 5.02 (1H, b), 4.52 (1H, d, J=9.3 Hz), 4.42 (1H, t, J=7.1 Hz), 3.98 (1H, dt, J= 8.5, 7.8 Hz), 2.93 (2H, m), 2.88

(1H, b), 2.68 (1H, m), 2.41 (1H, m), 2.24 (1H, m), 1.92 (1H, m), 1.65 (3H,s), 1.58 (3H,s), 1.37 (9H, s).

METHOD D

5(S)-(1(S)-AMINO-2-PHENYL-ETHYL)-3(R)-(3-FLUORO-3-METHYL-BUTYL)-DIHYDRO- FURAN-2-ONE

To a solution of product from Method C (9.81 g, 26.3 mmol) in dry benzene (300 mL) was added HF•pyridine (88 mL). The resulting solution was stirred at ambient temperature for 4 hours, then transferred to a 4 L beaker. To this was added ice, and the pH was slowly adjusted to 8-9 by addition of 2 M aqueous sodium hydroxide ($NaOH_{aq}$). The mixture was extracted with ethyl acetate (EtOAc) and the organics dried over magnesium sulfate, and then filtered and concentrated. Chromatography on silica gel yielded the title compound (5.68 g, 74%).

METHOD E

QUINOXALINE-2-CARBOXYLIC ACID {1(S)-[4(R)-(3-FLUORO-3-METHYL-BUTYL)-5-OXO-TETRAHYDRO-FURAN-2(S)-YL]-2-PHENYL-ETHYL)-AMIDE

To a solution of quinoxaline carboxylic acid (5.05 g, 29.0 mmol) in methylene chloride (100 mL) was added dimethylaminopyridine (DMAP) (3.55 g, 29.0 mmol) and EDCI (5.55 g, 29.0 mmol). The solution was stirred 10 minutes, then the product from Method D, above, (5.68 g, 19.4 mmol) was added in one portion. The solution was stirred for 12 hours, then diluted with diethyl ether and washed with saturated aqueous brine. The organics were dried over magnesium sulfate, and then filtered and concentrated. The crude product was purified by silica gel chromatography to yield the title compound (5.62 g, 64%).

METHOD F

QUINOXALINE-2-CARBOXYLIC ACID (1(S)-BENZYL-4(R)-BENZYLCARBAMOYL-7-FLUORO-2(S)-HYDROXY-7-METHYL-OCTYL)-AMIDE

To a solution of the product from Method E (0.10 g, 0.22 mmol) in dioxane (2 mL) was added glacial acetic acid (0.038 mL, 0.66 mmol) and benzylamine (approx. 1 mL, excess). The resulting solution was warmed to reflux for 1 hour, cooled to ambient temperature and diluted with water. The solution was extracted with ethyl acetate and the combined organics were dried over magnesium sulfate ($MgSO_4$), filtered and concentrated. Chromatography on silica gel, followed by recrystallization from methylene chloride/hexanes gave the title compound (0.068 g, 56%). m.p. 183 -184 °C.

EXAMPLE 3

METHOD F'

QUINOXALINE-2-CARBOXYLIC ACID (1-BENZYL-7-FLUORO-2-HYDROXY-4-HYDROXYCARBAMOYL-7-METHYL-OCTYL)-AMIDE

Hydroxylamine hydrochloride (1.55g, 22.4 mmol) and KOH (1.51g, 26.7 mmol) were combined in anhydrous methanol (20 mL) and stirred for 30 minutes under a dry nitrogen atmosphere, and then filtered. To the resulting filtrate was added the product from Method E (500 mg, 1.17 mmol) and the reaction mixture was stirred for 16 hours at room temperature. The solvent was removed in vacuo and the residue solvated in EtOAc (50 mL) and transferred to a separated funnel. The organic layer was washed with water and brine and dried (MgSO4). After filtration the solvent was removed in vacuo and the remaining residue recrystallized (methylene chloride/Hexanes) to give a pale yellow solid (330 mg, 58%) m.p. 165-166°C

EXAMPLE 4

QUINOXALINE-2-CARBOXYLIC ACID (1(S)-BENZYL-4(R)-CARBAMOYL-2(S)-HYDROXY-7-METHYL-OCTYL)-AMIDE

METHOD G

ALKENE HYDROGENATION

{1(S)-[4(R)-(3-METHYL-BUTYL)-5-OXO-TETRAHYDRO-FURAN-2(S)-YL]-2-PHENYL-ETHYL)-CARBAMIC ACID TERT-BUTYL ESTER

The product from Method C, from Example 2 above, (3.0 g, 8.04 mmol) was placed in a 250 mL Parr Shaker bottle and dissolved in ethanol (50 mL). Under a nitrogen atmosphere, Palladium (Pd) on activated carbon (0.30 g, 10% Pd content) was added to the solution. The mixture was placed on a Parr Shaker hydrogenator at 50 psi for 5 hours at room temperature. The hydrogenation mixture was diluted with ethyl acetate and then poured through a Celite® pad while washing copiously with ethyl acetate. The solvent of the filtrate was removed *in vacuo* to yield the title compound, 2.63 g (88%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (5H, m), 4.54 (1H, d, *J*=9.8 Hz), 4.46 (1H, t, *J*=6.9), 4.0 (1H, dt), 2.89 (2H, d, *J*=8.1), 2.57 (1H, m), 2.32 (1H, b), 1.89 (1H, m), 1.79 (1H, m), 1.52 (2H, m), 1.37 (9H, s), 1.23 (2H, m), 0.86 (6H, d, *J*=6.6 Hz).

The product from Method G was converted into the title compound by procedures analogous to those of Methods A and B except that quinoline-3-carboxylic acid is replaced with quinoxaline-2-carboxylic acid and methylamine is replaced with ammonia gas to yield 0.095 g (72%) of the title compound.

^{1}H NMR (400 MHz, $CDCl_3$) : δ 9.61(1H, s), 8.32 (1H, d, *J*=8.9 Hz), 8.16 (2H, m), 7.86 (2H,m), 7.28 (10H, m), 7.19 (1H, m), 5.70 (1H, b), 5.29 (1H, b), 4.27 (1H, m), 8.21 (1H, d, *J*=4.4 Hz), 3.91 (1H, m), 3.11 (2H, m), 2.46 (1H, m), 1.74 (1H, t, *J*=6.4 Hz), 1.61 (1H, m), 1.42 (2H, m), 1.17 (1H, m), 1.09 (1H, m), 0.81 (3H, d, *J*=7.1 Hz), 0.79 (3H, d, *J*=7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) :d 179.11, 163.73, 143.90, 143.76, 143.15, 140.28, 137.96, 131.68, 130.84, 129.84, 129.44, 129.25, 128.58, 126.60, 68.55, 55.90, 43.44, 38.39, 36.90, 36.70, 29.77, 28.03, 22.42

EXAMPLE 5

QUINOXALINE-2-CARBOXYLIC ACID 1(S)-BENZYL-4(R)-CARBAMOYL-2(S)-HYDROXY-7,7-DIMETHYL-OCTYL)-AMIDE

METHOD H

TRIFLATE ALKYLATION

{1-[4-(3,3-DIMETHYL-BUTYL)-5-OXO-TETRAHYDRO-FURAN-2-YL]-2-PHENYL-ETHYL}-CARBAMIC ACID TERT-BUTYL ESTER

To a flame dried round bottom flask under a nitrogen atmosphere was added terahydrofuran (THF) (2 mL) and 1,1,1,3,3,3 hexamethyldisilazane (0.82 mL, 3.88 mmol). The mixture was cooled to 0°C and n-butyl lithium (1.48 mL of a 2.5 M solution in hexanes, 3.72 mmol) was added dropwise via syringe. The mixture was stirred for 15 minutes and then cooled to -78°C. {1(S)-[5-Oxo-tetrahydro-furan-2(S)-yl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester (0.52 g, 1.69 mmol prepared by the method of Fray, supra) dissolved in tetrahydrofuran (2 mL) was slowly added to the solution via syringe and the solution was stirred for 1 hour. A solution of the desired triflate, i.e. 3,3-dimethylbutyl triflate (0.92 g, 3.37 mmol)(prepared according to the method of Beard, et al., J Org Chem., *38*, 3673 (1973)) in tetrahydrofuran (2 mL) was added dropwise via syringe and the mixture was stirred for 2 hours at -78°C. The mixture was quenched by addition of saturated aqueous ammonium chloride (NH_4Cl) (25 mL). Upon warming to room temperature, the mixture was diluted with ethyl acetate (40 mL), transferred to a separatory funnel, and washed with saturated aqueous NH_4Cl (2x40 mL), saturated $NaHCO_3$ (2x40 mL), and brine (40 mL). The organic layers were dried ($MgSO_4$) and the solvent removed under reduced pressure. The resulting crude oil was chromatographed on silica gel (25g) eluting with 100 mL 5:1 hexanes/ethyl acetate followed by 400 mL 4:1 hexanes/ethyl acetate. This provided 0.36 g (50%) of the title compound.

TLC: (4:1 hexanes/ethyl acetate) R_f: 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) :δ 7.25 (m, 7H), 6.92 (t, 1H, J= 7.5 Hz), 6.85 (d, 2H, J= 8.1 Hz), 4.67 (d, 2H, J= 6.0 Hz), 4.49 (t, 1H, J=

9.6 Hz), 4.06 (m, 3H), 2.89 (m, 3H), 2.43 (m, 1H), 2.26 (m, 1H), 2.05 (m, 1H), 1.95 (m, 1H), 1.37 (s, 9H).

The product of Method H was converted to the title compound by procedures analogous to those of Methods A and B, from Example 1, except that quinoline-3-carboxylic acid is replaced with quinoxaline-2-carboxylic acid and methylamine is replaced with ammonia gas.

EXAMPLE 6

QUINOXALINE-2-CARBOXYLIC ACID [1(S)-BENZYL-4(S)-CARBAMOYL-2(S)-HYDROXY-4-(1-HYDROXY-CYCLOHEXYL)-BUTYL]-AMIDE AND

QUINOXALINE-2-CARBOXYLIC ACID [1(S)-BENZYL-4(R)-CARBAMOYL-2(S)-HYDROXY-4-(1-HYDROXY-CYCLOHEXYL)-BUTYL]-AMIDE

METHOD I

{1(S)-[4(S)-(1-HYDROXY-CYCLOHEXYL)-5-OXO-TETRAHYDRO-FURAN-2(S)-YL]-2-PHENYL-ETHYL}-CARBAMIC ACID TERT-BUTYL ESTER

To a solution of diisopropylamine (0.90 mL, 6.88 mmol) in THF (10 mL) at 0°C was added a solution of n-butyl lithium (2.7 mL, 6.71 mmol, 2.5 M in hexanes). The solution was stirred for 15 minutes, then cooled to - 78 °C. To this was added dropwise a solution of {1(S)-[5-Oxo-tetrahydro-furan-2(S)-yl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester (1.0 g, 3.27 mmol prepared as in example 2, method C) in tetrahydrofuran (10 mL) and the reaction was stirred an additional 30 minutes. To this was added the appropriate ketone, e.g., cyclohexanone) (0.37 mL, 3.60 mmol), and the solution was warmed to ambient temperature. The reaction was quenched by addition of saturated aqueous bicarbonated $NaHCO_3$) solution and the mixture extracted with diethyl ether. The combined organics were dried over magnesium sulfate (MgSO4), filtered and concentrated. Chromatography on silica gel gave a mixture of separable diastereomers of {[1(S)-[4(S)-(1-hydroxy-cyclohexyl)-5-oxo-tetrahydro-furan-2(S)-yl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester (0.687 g) and {1(S)-[4(R)-(1-hydroxy-cyclohexyl)-5-oxo-tetrahydro-furan-2(S)-yl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester (0.269 g) in 67 % overall yield.

The products from Method I were converted to the title compounds by procedures analogous to those of Methods A and B, from Example 1, except that quinoline-3-carboxylic acid is replaced with quinoxaline-2-carboxylic acid and methylamine is replaced with ammonia gas.

EXAMPLE 7

FLUORO-QUINOLINE-3-CARBOXYLIC ACID (1(S)-BENZYL-4(S)-CARBAMOYL-4-CYCLOHEXYL-2(S)-HYDROXY-BUTYL)-AMIDE AND FLUORO-QUINOLINE-3-CARBOXYLIC ACID (1(S)-BENZYL-4(R)-CARBAMOYL-4-CYCLOHEXYL-2(S)-HYDROXY-BUTYL)-AMIDE

METHOD J

{1(S)-[4(S)-(1-HYDROXY-CYCLOHEXYL)-5-OXO-TETRAHYDRO-FURAN-2(S)-YL]-2-PHENYL-ETHYL}-CARBAMIC ACID TERT-BUTYL ESTER

To a solution of the title compound from Method I, Example 5, (1.38 g, 3.42 mmol) in benzene (40 mL) was added (methoxycarbonylsulfamoyl)-triethylammonium hydroxide, inner salt (Burgess reagent) (1.30 g, 5.47 mmol) and the solution was warmed to reflux for 2 hours. The reaction was diluted with diethyl ether and washed with saturated aqueous brine. The organics were dried over magnesium sulfate, filtered and concentrated to give the crude elimination product. This was directly dissolved in 5:1 tetrahydrofuran/methanol (THF/MeOH)(30 mL) and transferred to a Parr flask containing 10% palladium on carbon (Pd/C) (1 g). The mixture was hydrogenated at 35 psi for 1.5 hours, then filtered through a pad of Celite and the filtrate concentrated. Chromatography on silica gel yielded the title compound as a mixture of separable diastereomers {1(S)-[4(S)-(1-hydroxy-cyclohexyl)-5-oxo-tetrahydro-furan-2(S)-yl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester (0.53 g) and {1(S)-[4(R)-(1-hydroxy-cyclohexyl)-5-oxo-tetrahydro-furan-2(S)-yl]-2-phenyl-ethyl}-carbamic acid tert-butyl ester (0.29 g) in 62 % overall yield.

The products from Method J were converted to the title compounds by procedures analogous to those of Methods A and B, from Example 1, except that quinoline-3-carboxylic acid is replaced with quinoxaline-2-carboxylic acid and methylamine is replaced with ammonia gas.

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The compounds from Table 1 were prepared according to the methods described above, substituting where appropriate the correct R^2 aldehyde, R^3 group (such as allylic halide, alkyl triflate, ketone, etc.), R^1 carboxylic acid or R^4 and R^5 amine where appropriate.

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TABLE 1

EXAMPLE	NAME	M.P. (°C)	LRMS
8.	Quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide		455
9.	Quinoxaline-2-carboxylic acid (6-chloro-1-cyclohexylmethyl-2(S)-hydroxy-4(S)-methylcarbamoyl-hept-6-enyl)-amide		
10.	Quinoline-3-carboxylic acid (2(S)-hydroxy-1(S)-isobutyl-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	155-157	414
11.	Quinoxaline-2-carboxylic acid 1(S)-sec-butyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	69-71	415
12.	Quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-hept-6-enyl)-amide		452
13.	Quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-hept-6-enyl)-amide		453
14.	N-1(S)-Cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-5-phenyl-nicotinamide	115-119	
15.	Quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	162-163	
16.	Quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-4(R)-dimethylcarbamoyl-2(S)-hydroxy-6-methyl-hept-6-enyl)-amide		467
17.	Quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide	171-175	453, 436
18.	Quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide		455, 437
19.	Isoquinoline-4-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide	180-182	454
20.	Quinoline-3-carboxylic acid (4(R)-carbamoyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-heptyl)-amide	186-188	440, 478, 423

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
21.	Quinoline-3-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	170.5-172.5	494
22.	Quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide		454
23.	Quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide	200-201.5	454
24.	Quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-5-phenyl-pentyl)-amide	199-200.5	488
25.	Quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-5-phenyl-pentyl)-amide	109-110.5	489
26.	Quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide	142-144	490, 417
27.	Quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-cyclobutylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide	148-150	488, 417
28.	Quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-benzylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide	158-162	524, 417
29.	Quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-cyclopropylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide	174-179	474
30.	Quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide	190-192.5	448
31.	Quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-ethylcarbamoyl-2(S)-hydroxy-6-methyl-heptyl)-amide	175-176	462
32.	Quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-propylcarbamoyl-heptyl)-amide		476
33.	Quinoline-3-carboxylic acid [1-benzyl-2(S)-hydroxy-4(R)-(2-hydroxy-ethylcarbamoyl)-6-methyl-heptyl]-amide	158-162	478
34.	Cinnoline-4(R)-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	185-186.5	449

TABLE 1

EXAMPLE	NAME	M.P. (°C)	LRMS
35.	Isoquinoline-4-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	200-201	448
36.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	166-167	449
37.	N-1(S)-Benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-5-bromo-nicotinamide	184.5-185.5	478
38.	Quinoline-3-carboxylic acid 1(R)-cyclohexylmethyl-2(R)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide		454
39.	Quinoxaline-2-carboxylic acid [1(S)-(4-benzyloxy-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide,	196-197	554
40.	Quinoline-3-carboxylic acid [1(S)-(4-benzyloxy-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide	178-179	555
41.	Isoquinoline-1-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	178-179	448
42.	Quinoline-4-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	189-192	448
43.	Quinoline-6-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	165-167	448
44.	Quinoline-3-carboxylic acid [2(S)-hydroxy-1(S)-(4-hydroxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide	220.5-222.5	464
45.	Quinoline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	160-161.5	449
46.	Naphthalene-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	218-220	447
47.	Quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclohex-1-enyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	172-174	486
48.	Quinoline-3-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-(3-methyl-butylcarbamoyl)-heptyl]-amide	153-154	504

TABLE 1

EXAMPLE	NAME	M.P. (°C)	LRMS
49.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(S)-methylcarbamoyl-heptyl)-amide	157-163	449
50.	Trifluoro-methanesulfonic acid 4-{3(S)-hydroxy-7-methyl-5(R)-methylcarbamoyl-2(S)-[(quinoline-3-carbonyl)-amino]-octyl}-phenyl ester	168-170	596
51.	Trifluoro-methanesulfonic acid 4-{3(S)-hydroxy-7-methyl-5(R)-methylcarbamoyl-2(S)-[(quinoxaline-2-carbonyl)-amino]-octyl}-phenyl ester		597
52.	Quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	185-187	488
53.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	132-134	489, 471
54.	Isoquinoline-3-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	150.5-151.5	488
55.	N-1(S)-Benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-5-bromo-nicotinamide	199-200.5	518
56.	Quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-prop-2-ynylcarbamoyl-heptyl)-amide		472
57.	Quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-hydroxycarbamoyl-6-methyl-heptyl)-amide		456, 438, 423
58.	Quinoline-3-carboxylic acid 2(S)-hydroxy-1(S)-(4-methoxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide	176-177	478
59.	Isoquinoline-3-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide,	205-207	494
60.	5-Bromo-N-(5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-nicotinamide	173.5-175	444
61.	Quinoxaline-2-carboxylic acid [2(S)-hydroxy-1(S)-(4-methoxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide		479
62.	Isoquinoline-4-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	220.5-224	494

TABLE 1

EXAMPLE	NAME	M.P. (°C)	LRMS
63.	Quinoline-2-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	120-122	488
64.	Isoquinoline-4-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide,	177-180	488
65.	Quinoxaline-2-carboxylic acid [2(S)-hydroxy-1(S)-(4-hydroxy-benzyl)-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide,	170-172	465
66.	Quinoxaline-2-carboxylic acid (5-cyclohexyl-1(S)-cyclohexylmethyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide		496
67.	Quinoline-3-carboxylic acid [1(S)-(4-chloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide	212.5-213.5	482
68.	Quinoxaline-2-carboxylic acid [1(S)-(4-chloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide		483
69.	Quinoline-3-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	173.5-175	468, 450
70.	Quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	78-80	470
71.	Quinoline-3-carboxylic acid [1(S)-(4-chloro-benzyl)-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide	198-201	522
72.	Quinoxaline-2-carboxylic acid [1(S)-(4-chloro-benzyl)-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide		523
73.	Quinoline-2-carboxylic acid [1(S)-(4-chloro-benzyl)-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide		522
74.	Benzofuran-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	181-183	437
75.	N-1(S)-Benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-5,6-dichloro-nicotinamide	195-196	466, 432

TABLE 1

EXAMPLE	NAME	M.P. (°C)	LRMS
76.	Quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	188-190	462
77.	N-1(S)-Benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-5-bromo-nicotinamide	188-189	490
78.	5,6,7,8-Tetrahydro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	142.5-144.5	452
79.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	147-149	463
80.	Quinoline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide,	156-158	462
81.	Isoquinoline-4-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	199-202	462
82.	Quinoxaline-2-carboxylic acid [1(S)-(3,4-dichloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide		517, 483
83.	Benzo[b]thiophene-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	179-181	453
84.	2-Methyl-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	225-226.5	462
85.	6,7-Dimethoxy-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	211-214	508
86.	6,7-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	187-189	484, 466
87.	1H-Benzoimidazole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	136-140	437
88.	5-Methyl-pyrazine-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	171.5-172.5	413
89.	Quinoline-3-carboxylic acid [1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide	184-186	466
90.	Quinoxaline-2-carboxylic acid [1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide	153-156	467

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
91.	5-Chloro-1H-indole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	245-247	470
92.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	194-194.5	449, 432
93.	2-Methoxy-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide,	175-181	478
94.	5,6-Dichloro-1H-benzoimidazole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	114-117	505
95.	Benzothiazole-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	86-89	454
96.	7,8-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	179-182	484
97.	6,7,8-Trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	156-161	502, 484
98.	5,8-Dimethyl-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	197-199	476
99.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	103-106	505
100.	Quinoline-3-carboxylic acid [1(S)-(3,4-dichloro-benzyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide		516
101.	5,6,7,8-Tetrahydro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	169.5-172.5	466
102.	Quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	176-178	474
103.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide	120-122	475
104.	N-1(S)-Benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-5-bromo-nicotinamide	194-198	504

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
105.	5,6,7,8-Tetrahydro-quinoline-3-carboxylic acid 1(S)-benzyl-5-cyclopentyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide,	143-146	478
106.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-5-cyclopentyl-2(S)-hydroxy-pentyl)-amide	217-219	461, 444
107.	6,7-Dihydro-5H-[1]pyrindine-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	154.5-156	452, 349
108.	Quinoxaline-2-carboxylic acid [1(S)-(4,4-difluoro-cyclohexylmethyl)-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl]-amide	95-98	491, 473
109.	Quinoxaline-2-carboxylic acid [1(S)-(4,4-difluoro-cyclohexylmethyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide	95-98	506, 488
110.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-ethylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	129-133	478
111.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-propylcarbamoyl-octyl)-amide	125-130	492
112.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-cyclopropylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	168-169	490, 472
113.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-cyclobutylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	148-150	504, 486
114.	Quinoxaline-2-carboxylic acid [1(S)-(4-difluoromethoxy-benzyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide	151-154	530
115.	4-{3(S)-Hydroxy-7-methyl-5(R)-methylcarbamoyl-2(S)-[(quinoxaline-2-carbonyl)-amino]-octyl}-benzoic acid methyl ester	87-95	508
116.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4-carbamoyl-2(S)-hydroxy-butyl)-amide		379
117.	6,7,8-Trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	206-207	516, 498

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
118.	6,7,8-Trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	205-206	502, 485
119.	6,8-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	198-200	498
120.	6,8-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	188-190	484, 467
121.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-5-cyclopentyl-2(S)-hydroxy-pentyl)-amide	102-104	517, 499
122.	6-Methyl-pyridine-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	74-76	
123.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-8-methyl-4(R)-methylcarbamoyl-nonyl)-amide	145.5-146.5	477
124.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-8-methyl-nonyl)-amide	163-165	463
125.	Quinoxaline-2-carboxylic acid 1(S)-biphenyl-4-ylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	123-125	539, 521, 508
126.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-oct-6-enyl)-amide	168-170	447, 430
127.	Quinoxaline-2-carboxylic acid (2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-1(S)-naphthalen-2-ylmethyl-heptyl)-amide	121-123	
128.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7,7-dimethyl-octyl)-amide	77-79	463, 446
129.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7,7-dimethyl-4(R)-methylcarbamoyl-octyl)-amide	195-199	477, 459
130.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide	168-172	469, 452
131.	Quinoxaline-2-carboxylic acid 1(S)-biphenyl-4-ylmethyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	205-206	508
132.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-5-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl]-amide	170-172	525, 507

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
133.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-pentyl]-amide	174-176	511, 493
134.	Quinoxaline-2-carboxylic acid [1(S)-(3-fluoro-benzyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide	158.5-159.5	481, 463
135.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide	191-191.5	467, 449
136.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-oct-6-enyl)-amide	65-68	461, 443
137.	6,7,8-Trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7(S)-methyl-4(R)-methylcarbamoyl-nonyl)-amide	158-161	541, 523
138.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7(S)-methyl-nonyl)-amide	185-187	446
139.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	148-150	482, 463
140.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	184-186	467, 449
141.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-nonyl)- amide	137-139.5	478
142.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-dimethylcarbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	68-70	
143.	7,8-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-4(R)-methylcarbamoyl-5-phenyl-pentyl)-amide	175 (Dec.)	518, 500
144.	7,8-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	198-201	498, 480
145.	8-Fluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide	179-183	480, 462
146.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-4(R)-methylcarbamoyl-non-6-enyl)-amide	130-132	462, 448

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
147.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-non-6-enyl)-amide	154-155	448, 430
148.	7,8-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	188-190	485, 467
149.	8-Fluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-7-methyl-octyl)-amide	192-196	466, 449
150.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-nonyl)-amide	188.5-189.5	450
151.	2(S)-{2(S)-hydroxy-4-phenyl-3(S)-[(quinoxaline-2-carbonyl)-amino]-butyl}-N1,N4-dimethyl-succinamide	178-180	
152.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-ethylcarbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	105-108	496
153.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-butylcarbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	110-112	523, 505
154.	Quinoxaline-2-carboxylic acid [7-fluoro-1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl]-amide	145-147	499
155.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3,4-dichloro-benzyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide	206-207	536, 518
156.	7,8-Difluoro-quinoline-3-carboxylic acid [4(R)-carbamoyl-1(S)-(3,4-dichloro-benzyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide	187-189	571
157.	Quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-phenethyl-octyl)-amide,	223-225	478
158.	7,8-Difluoro-quinoline-3-carboxylic acid [4(R)-carbamoyl-7-fluoro-1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide	208-210	463, 445
159.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-1(S)-(4-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide		520
160.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(4-methyl-piperazine-1-carbonyl)-octyl]-amide,		551

TABLE 1

EXAMPLE	NAME	M.P. (°C)	LRMS
161.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(tetrahydro-pyran-4(R)-yl)-pentyl]-amide	212-214	477, 459
162.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(piperidine-1-carbonyl)-octyl]-amide		536
163.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(morpholine-4-carbonyl)-octyl]-amide,		537
164.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-3-(2-carbamoyl-indan-2-yl)-2(S)-hydroxy-propyl]-amide	90-100	481, 464
165.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-4(R)-methylcarbamoyl-7-phenyl-hept-6-enyl)-amide	212-216 (Dec.)	
166.	Quinoline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	163.5-165	466, 449
167.	6,7-Dihydro-5H-[1]pyrindine-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	175-178	456
168.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclohexyl-2(S)-hydroxy-butyl)-amide;	222-223	461, 444
169.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclohexyl-2(S)-hydroxy-butyl)-amide	178-180	461, 444
170.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclohexyl-2(S)-hydroxy-butyl)-amide	229-232	447
171.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4-carbamoyl-4(S)-cyclopentyl-2(S)-hydroxy-butyl)-amide;	126-128	447
172.	Quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	200-202	466. 449
173.	N-1(S)-Benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-5-bromo-nicotinamide	181-183	476
174.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1-(2(S)-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide	184-187	466, 448
175.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(2-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide	213-215	466

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
176.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(4-isopropyl-cyclohexyl)-butyl]-amide;		502
177.	Quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiophen-2-ylmethyl-octyl)-amide		454, 436
178.	Quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiazol-4-ylmethyl-octyl)-amide	195-196	456
179.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(3,3,5,5-tetramethyl-cyclohexyl)-butyl]-amide	188-190	516
180.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-indan-2-yl-butyl)-amide;		495
181.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cycloheptyl-2(S)-hydroxy-butyl)-amide;	216-217	474, 457
182.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-5-propyl-octyl)-amide;		477
183.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-5-propyl-oct-5-enyl)-amide;		
184.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide		
185.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-7-chloro-2(S)-hydroxy-4(R)-methylcarbamoyl-hept-6-enyl)-amide		467, 449
186.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-7-chloro-2(S)-hydroxy-4(R)-methylcarbamoyl-hept-6-enyl)-amide		467, 449
187.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-6-chloro-2(S)-hydroxy-4(S)-methylcarbamoyl-hept-6-enyl)-amide	160-162	467, 449
188.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-6-chloro-2(S)-hydroxy-hept-6-enyl)-amide	203-204.5	
189.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(S)-carbamoyl-6-cyclopropyl-2(S)-hydroxy-hexyl)-amide	171-174	447, 429

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
190.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-6-cyclopropyl-2(S)-hydroxy-4(R)-methylcarbamoyl-hexyl)-amide	146-148	461, 443
191.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-4(S)-(4-methyl-cyclohexyl)-butyl]-amide;	218-220	475, 457
192.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-indan-2-yl-butyl)-amide;	190-191	495, 477
193.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(4-trifluoromethoxy-phenyl)-pentyl]-amide	184-187	553, 536
194.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(4-fluoro-phenyl)-2(S)-hydroxy-pentyl]-amide	164-166	487, 470
195.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-hept-6-enyl)-amide	165-166	436
196.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-hept-6-enyl)-amide	158-160	436
197.	3-Hydroxy-quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	185-189	483, 465
198.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-benzylcarbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	183-184	
199.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(pyridin-3-ylmethyl)-carbamoyl]-octyl}-amide	188-191	
200.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-8,8-trifluoro-2(S)-hydroxy-4(R)-methylcarbamoyl-7-trifluoromethyl-octyl)-amide		571, 553
201.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-8,8-trifluoro-2(S)-hydroxy-7-trifluoromethyl-octyl)-amide	187-193	553
202.	Quinoxaline-2-carboxylic acid [2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-1(S)-(4-methylcarbamoyl-benzyl)-octyl]-amide	170-173	502

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
203.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-5-ethyl-2(S)-hydroxy-heptyl)-amide;	215-218	448, 431
204.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(tetrahydro-pyran-4-yl)-butyl]-amide;	151-154	
205.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2-pyridin-2-yl-ethylcarbamoyl)-octyl]-amide	155-156	572
206.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-(3,4-dimethoxy-benzylcarbamoyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide	162-164	617
207.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-6-methoxy-hexyl)-amide		420
208.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-oct-6-enyl)-amide	172-175	450
209.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-7-chloro-2(S)-hydroxy-4(R)-methylcarbamoyl-oct-6-enyl)-amide	108-111	463
210.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-4-(3,5-dimethyl-cyclohexyl)-2(S)-hydroxy-butyl]-amide;	221-222	489, 471
211.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(pyridin-2-ylmethyl)-carbamoyl]-octyl}-amide	138-140	557, 540
212.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-[2-(4-hydroxy-phenyl)-ethylcarbamoyl]-7-methyl-octyl}-amide	138-140	587, 569
213.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(thiophen-2-ylmethyl)-carbamoyl]-octyl}-amide	174-175	563, 545
214.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-6-phenoxy-hexyl)-amide	194.5-196.5	482
215.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-6-isopropoxy-hexyl)-amide	113-118 (Mix)	448
216.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[2-(4-sulfamoyl-phenyl)-ethylcarbamoyl]-octyl}-amide	207-210	650

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
217.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(pyridin-4-ylmethyl)-carbamoyl]-octyl}-amide	100-104	558
218.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-(2-ethylsulfanyl-ethylcarbamoyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide	78-79	555, 537
219.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(2-methoxy-ethylcarbamoyl)-7-methyl-octyl]-amide	48-50	507
220.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2-pyridin-3-yl-ethylcarbamoyl)-octyl]-amide	154-155	572
221.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2-pyridin-4-yl-ethylcarbamoyl)-octyl]-amide	78-80	572
222.	Quinoxaline-6-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	190-192	467
223.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-6-tert-butoxy-4(R)-carbamoyl-2(S)-hydroxy-hexyl)-amide	184-189	479, 461
224.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[2-1-methyl-1H-pyrrol-2-yl)-ethylcarbamoyl]-octyl}-amide	100-105	574
225.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(1,1-dioxo-thiopyran-4-yl)-2(S)-hydroxy-butyl]-amide;	140-150	511, 494
226.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-[2-(6-methoxy-1H-indol-3-yl)-ethylcarbamoyl]-7-methyl-octyl}-amide,		640, 622
227.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(2-methoxy-benzylcarbamoyl)-7-methyl-octyl]-amide	135	587, 569
228.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(3-methoxy-benzylcarbamoyl)-7-methyl-octyl]-amide		587, 569
229.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(2-thiophen-2-yl-ethylcarbamoyl)-octyl]-amide	152-154	577

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
230.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-[2-(1H-indol-3-yl)-ethylcarbamoyl]-7-methyl-octyl}-amide	107-108	610
231.	Quinoxaline-2-carboxylic acid {4(R)-[2-(4-amino-phenyl)-ethylcarbamoyl]-1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide		586
232.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-4(R)-[2-(3,5-dimethoxy-phenyl)-ethylcarbamoyl]-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide	109-112	631, 613
233.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-4(R)-[2-(3,4-dimethoxy-phenyl)-ethylcarbamoyl]-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide		631, 613
234.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-4(R)-[(furan-2-ylmethyl)-carbamoyl]-2(S)-hydroxy-7-methyl-octyl}-amide	155.5-156.5	547
235.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-4(R)-[2-(2,5-dimethoxy-phenyl)-ethylcarbamoyl]-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide		631, 613
236.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(4-methoxy-benzylcarbamoyl)-7-methyl-octyl]-amide	114-115	587, 569
237.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-6-cyclohexyloxy-2(S)-hydroxy-hexyl)-amide	150-152	505, 487
238.	Quinoxaline-2-carboxylic acid {4(R)-[(1H-benzoimidazol-2-ylmethyl)-carbamoyl]-1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl}-amide		596
239.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-(2(S)-hydroxymethyl-pyrrolidine-1-carbonyl)-7-methyl-octyl]-amide	217-219	551, 533
240.	Quinoxaline-2-carboxylic acid {1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-[(tetrahydrofuran-2-ylmethyl)-carbamoyl]-octyl}-amide	111-115	551, 533
241.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-butyl]-amide	176-179	497, 478

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
242.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-(2,3-dimethoxy-benzylcarbamoyl)-7-fluoro-2(S)-hydroxy-7-methyl-octyl]-amide	99-101	
243.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclohexyl)-butyl]-amide;	187-189	477, 379
244.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(2,6-dimethyl-tetrahydro-pyran-4-yl)-2(S)-hydroxy-butyl]-amide;	195-198	491
245.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-1(S)-(3-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide	225-227	485, 467
246.	7,8-Difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	>220	502, 485
247.	N-1(S)-Benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-5,6-dichloro-nicotinamide	>220	484, 466
248.	Benzofuran-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	190-192	455, 438
249.	Cinnoline-4-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	198-199.5	469, 451
250.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-1(S)-(4-iodo-benzyl)-7-methyl-octyl]-amide,	185.5-187.5	593, 576
251.	Pyrazine-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide,	211-212	417, 319
252.	6,7,8-Trifluoro-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide,	195-197	520, 503
253.	Quinoline-6-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide,	170-173	466, 449
254.	Isoquinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide,	194-197	466, 448
255.	2-Methoxy-quinoline-3-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide,	213-216	496, 479

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
256.	1H-Benzoimidazole-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide,	168-169	456, 438
257.	Benzothiazole-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	152.5-155	472, 455
258.	5-Methyl-pyrazine-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide	194-197	431
259.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-pyridin-3-yl-pentyl)-amide		470, 453
260.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclohexyl)-butyl]-amide;	210-211	477, 459
261.	Quinoline-3-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide	231	460, 443
262.	Quinoline-2-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide	208-210	460, 443
263.	Fluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide	238-240	478, 461
264.	N-(1(S)-Benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-5,6-dichloro-nicotinamide;	174-177	461
265.	N-(1(S)-Benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-5-bromo-nicotinamide;	255-256	475, 458
266.	Quinoxaline-2-carboxylic acid (4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-1(S)-phenyl-octyl)-amide,	159-160.5	453
267.	Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-pyridin-2-yl-pentyl)-amide,		470, 453
268.	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclohexyl)-1(S)-thiophen-2-ylmethyl-butyl]-amide;	206-207	482
269.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(4-hydroxy-tetrahydro-thiopyran-4-yl)-butyl]-amide;	123-125	495, 379
270.	1,3-Dimethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide,	189.5-191	484, 467

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
271.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl)-amide	165-166	
272.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-7-fluoro-2(S)-hydroxy-4(R)-methoxycarbamoyl-7-methyl-octyl)-amide		
273.	7,8-Difluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide	233-235	
274.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(2-chloro-phenyl)-2(S)-hydroxy-pentyl]-amide	182-185	
275.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-o-tolyl-pentyl)-amide	168-171	
276.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-2(S)-hydroxy-4(R)-hydroxycarbamoyl-5-phenyl-pentyl)-amide	190-192	
277.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cyclopentyl)-butyl]-amide	192-195	463, 446
278.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide	230-233	490
279.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-5-(3,4-dichloro-phenyl)-2(S)-hydroxy-pentyl]-amide	199-201	
280.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(2-fluoro-phenyl)-2(S)-hydroxy-pentyl]-amide	171-173	
281.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-cyclopentyl)-butyl]-amide	110-112	477
282.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-3-methyl-cyclopentyl)-butyl]-amide	187-188	476
283.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide	114-116	506
284.	N-(1(S)-Benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-5-bromo-nicotinamide		494, 496

TABLE 1

EXAMPLE	NAME	M.P. (°C)	LRMS
285.	8-Fluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide	206-209	
286.	6,7-Dihydro-5H-[1]pyrindine-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide	182-186	
287.	Quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide	203-206	
288.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-3,5-dimethyl-cyclohexyl)-butyl]-amide	234-236	504
289.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-3,5-dimethyl-cyclohexyl)-butyl]-amide		520
290.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-cycloheptyl)-butyl]-amide	189-191	491
291.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-cycloheptyl)-butyl]-amide	118-119	506
292.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-5-(3-fluoro-phenyl)-2(S)-hydroxy-pentyl]-amide	176-179	
293.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-m-tolyl-pentyl)-amide	178-179	
294.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-2(S)-hydroxy-4-isobutylcarbamoyl-butyl)-amide	146-148	
295.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(2-hydroxy-adamantan-2-yl)-butyl]-amide	206-207	528
296.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(9-hydroxy-bicyclo[3.3.1]non-9-yl)-butyl]-amide	268-269	516
297.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-(2-hydroxy-adamantan-2-yl)-4-hydroxycarbamoyl-butyl]-amide	133-134	544
298.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-(9-hydroxy-bicyclo[3.3.1]non-9-yl)-4-hydroxycarbamoyl-buty l]-amide	130-132	532

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
299.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(3-methoxy-phenyl)-pentyl]-amide	147-148	
300.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4-propyl-cyclohexyl)-butyl]-amide	227-228	519
301.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4-propyl-cyclohexyl)-butyl]- amide	115-117	533
302.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-(4-methoxy-phenyl)-pentyl]-amide		500, 483
303.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4(S)-(4-ethyl-1-hydroxy-cyclohexyl)-2-hydroxy-butyl]-amide	246-248	504
304.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4,4-dimethyl-cyclohexyl)-butyl]-amide	210-211	505
305.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4,4-dimethyl-cyclohexyl)-but yl]-amide	118-123	520
306.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4-(4,4-difluoro-1-hydroxy-cyclohexyl)-2(S)-hydroxy-butyl]-amide	207.5-208.5	
307.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-(4,4-difluoro-1-hydroxy-cyclohexyl)-2(S)-hydroxy-4-hydroxycarbamoyl-but yl]-amide	130-131	572
308.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-2(S)-hydroxy-4-(1-hydroxy-4-trifluoromethyl-cyclohexyl)-butyl]-amide	250-252	545
309.	Quinoxaline-3- carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-6-methyl-4(R)-methylcarbamoyl-heptyl)-amide	94-98	454
310.	Quinoxaline-2-carboxylic acid [1(S)-benzyl-7-fluoro-2(S)-hydroxy-7-methyl-4(R)-(pyrrolidine-1-carbonyl)-octyl]-amide	174-175.5	522
311.	N-(1(S)-Benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-5-bromo-nicotinamide	218-220	470

TABLE 1			
EXAMPLE	NAME	M.P. (°C)	LRMS
312.	Quinoxaline-2-carboxylic acid (1(S)-benzyl-7-fluoro-4(R)-hydrazinocarbonyl-2(S)-hydroxyl-7-methyl-octyl)-amide	147-149	482,467

EXAMPLE 313

Quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S), 7-dihydroxy-7-methyloctyl)-amide

To the lactone from Example 2, method C (100 mg, 0.27 mmol), was added neat trifluoroacetic acid (1 mL). The resulting solution was stirred for 1 hour and the trifluoroacetic acid removed in vacuo. The remaining residue was solvated in methylene chloride (10 mL) and triethylamine (0.15 mL, 1.07 mmol). Quinoxalyl chloride (58 mg, 0.3 mmol) was added as a solid and the mixture stirred for 18 hour. The mixture was transferred to a separatory funnel and washed with citric acid (2x10 mL), $NaHCO_3$ (10 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$) and the solvents filtered. The filtrate was concentrated in vacuo and the resulting residue was chromatographed on silica gel (10 g) eluting with 2:1 hexanes:ethyl acetate to provide 99 mg of the quinoxaline amide. This material was solvated in methanol and ammonia gas was bubbled in for 5 minutes. The resulting solution was stirred for 16 hours and the solvent removed in vacuo. The remaining residue was recrystallized (methylene chloride/methanol/Hexanes) to provide the title compound (90 mg, 72%). 1H NMR (400 MHz, CD3OD): d 9.38 (1H, s), 8.21 (1H, dd, J=4.4, 2.5 Hz), 8.14 (1H, dd, J=4.4, 2.5 Hz), 7.93 (2H, m), 7.26 (2H, d, J=6.9 Hz), 7.17 (2H, t, J=7.1 Hz), 7.09 (1H, t, J=7.3 Hz), 4.30 (1H, m), 3.75 (1H, m), 3.03-2.98 (2H, m), 2.47 (1H, m), 1.77 (1H, m), 1.56 (2H, m), 1.4 (2H, m), 1.07 (6H, s).

EXAMPLES 314-344

The compounds from Table 2 were prepared according to the methods described above, substituting where appropriate the correct R^2 aldehyde, R^3 group, R^1 carboxylic acid or R^4 and R^5 amine where appropriate.

TABLE 2

EXAMPLE NUMBER	NAME	MP	LRMS
314	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide	153-155	483., 465., 448

EXAMPLE NUMBER	NAME	MP	LRMS
315	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3,5-difluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide	162-163	500, 483, 466
316	Quinoxaline-2-carboxylic acid 4(R)-carbamoyl-1(S)-(3-chloro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide	161-163	499, 481, 464
317	Quinoxaline-2-carboxylic acid [1(S)-(3-chloro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide	108-111	497, 464
318	7,8-Difluoro-quinoline-3-carboxylic acid (1S)-benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide	171-173	501, 484
319	6,7,8-Trifluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide	185-188	519, 502
320	Quinoxaline-2-carboxylic acid [1(S)-(3,5-difluoro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide	98-100	517
321	Quinoxaline-2-carboxylic acid (1(S)-benzyl-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl)-amide	108-110	482, 464, 447
322	7,8-Difluoro-quinoline-3-carboxylic acid (1(S)-benzyl-4(R)-ethylcarbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide		507, 484, 447
323	N-(1(S)-Benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-4-trifluoromethyl-nicotinamide	131-135	482, 464, 447
324	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(2-chloro-benzyl)-2(S),7-		

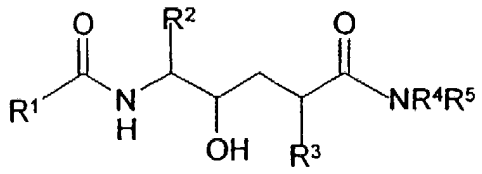
EXAMPLE NUMBER	NAME	MP	LRMS
	dihydroxy-7-methyl-octyl]-amide		
325	7,8-Difluoro-quinoline-3-carboxylic acid [(4R)-carbamoyl-1(S)-(3-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide	174-177	518
326	Quinoxaline-2-carboxylic acid [1(S)-(2-fluoro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide	130-131	499
327	Quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-1(S)-thiophen-2-ylmethyl-octyl)-amide	158-159	471, 453, 436
328	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(2-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide	147-148	483
329	Quinoxaline-2-carboxylic acid [1(S)-(3,4-difluoro-benzyl)-2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-octyl]-amide	150-153	517, 499, 466
330	Quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1(S)-(3,4-difluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide	110-120	501, 483, 466
331	Quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-1(S)-naphthalen-1-ylmethyl-octyl)-amide	155-158	515, 497, 480
332	6,7,8-Trifluoro-quinoline-3-carboxylic acid [4(R)-carbamoyl-1(S)-(3-fluoro-benzyl)-2(S),7-dihydroxy-7-methyl-octyl]-amide	183-185	536, 518
333	Quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-1(S)-naphthalen-2-ylmethyl-octyl)-amide	104-106	515, 497

EXAMPLE NUMBER	NAME	MP	LRMS
334	Quinoxaline-2-carboxylic acid (2(S),7-dihydroxy-4(R)-hydroxycarbamoyl-7-methyl-1(S)-naphthalen-2-ylmethyl-octyl)-amide	98-100	498, 480
335	Quinoxaline-2-carboxylic acid (1(S)-benzo[b]thiophen-3-ylmethyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyl-octyl)-amide	163-164	521, 503, 486
336	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(4-hydroxy-phenyl)-pentyl]-amide	190.5-191.5	
337	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(3-hydroxy-phenyl)-pentyl]-amide		
338	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(2-hydroxy-phenyl)-pentyl]-amide		
339	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(2-hydroxy-5-methyl-phenyl)-pentyl]-amide		
340	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(2-hydroxy-3-methyl-phenyl)-pentyl]-amide		
341	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-5-(3-ethoxy-2-hydroxy-phenyl)-2-hydroxy-pentyl]-amide		
342	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(4-hydroxy-3,5-dimethyl-phenyl)-pentyl]-amide		
343	Quinoxaline-2-carboxylic acid (1-benzyl-4-carbamoyl-2,6-dihydroxy-6-methyl-heptyl)-amide		

EXAMPLE NUMBER	NAME	MP	LRMS
344	Quinoxaline-2-carboxylic acid [1-benzyl-4-carbamoyl-2-hydroxy-5-(1-hydroxy-cyclohexyl)-pentyl]-amide		

CLAIMS

1. A compound of the formula



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wherein R^1 is (C_2-C_9)heteroaryl optionally substituted with one or more substituents independently selected from the group consisting of hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms, (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, $[(C_1-C_6)alkyl]_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, $[(C_1-C_6)alkyl]_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, $[(C_1-C_6)alkyl]_2N$-(C=O)-, $H_2N(C=O)$-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, $[(C_1-C_6)alkyl]_2N$-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, $H_2N-SO_2-(C_1-C_6)$alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, $[(C_1-C_6)alkyl]_2N-SO_2-(C_1-C_6)$alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

R^2 is phenyl-$(CH_2)_m$-, naphthyl-$(CH_2)_m$-, (C_3-C_{10})cycloalkyl-$(CH_2)_m$-, (C_1-C_6)alkyl or (C_2-C_9)heteroaryl-$(CH_2)_m$-, wherein m is an interger from zero to four; wherein each of said phenyl, naphthyl, (C_3-C_{10})cycloalkyl or (C_2-C_9)heteroaryl moieties of said phenyl-$(CH_2)_m$-, naphthyl-$(CH_2)_m$-, (C_3-C_{10})cycloalkyl-$(CH_2)_m$- or (C_2-C_9)heteroaryl-$(CH_2)_m$- groups may optionally be substituted with one or more substituents independently selected from hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms, (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl,

H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, phenoxy, benzyloxy, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

R^3 is hydrogen, (C_1-C_{10})alkyl, (C_3-C_{10})cycloalkyl-(CH_2)$_n$-, (C_2-C_9)heterocycloalkyl-(CH_2)$_n$-, (C_2-C_9)heteroaryl-(CH_2)$_n$- or aryl-(CH_2)$_n$-; wherein n is an interger from zero to six;

wherein said R^3 (C_1-C_{10})alkyl group may optionally be substituted with one or more substituents, independently selected from hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms, (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl; and wherein any of the carbon-carbon single bonds of said (C_1-C_{10})alkyl may optionally be replaced by a carbon-carbon double bond;

wherein the (C_3-C_{10})cycloalkyl moiety of said R^3 (C_3-C_{10})cycloalkyl-(CH_2)$_n$- group may optionally be substituted by one to three substitutents independently selected from the group consisting of hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms, (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-

$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

wherein the $(C_2$-$C_9)$heterocycloalkyl moiety of said R^3 $(C_2$-$C_9)$heterocycloalkyl-$(CH_2)_n$- group may contain from one to three heteroatoms independently selected from nitrogen, sulfur, oxygen, >S(=O), $>SO_2$ or $>NR^6$, wherein said $(C_2$-$C_9)$heterocycloalkyl moiety of said $(C_2$-$C_9)$heterocycloalkyl-$(CH_2)_n$- group may optionally be substituted on any of the ring carbon atoms capable of forming an additional bond with a substituent independently selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

wherein the $(C_2$-$C_9)$heteroaryl moiety of said R^3 $(C_2$-$C_9)$heteroaryl-$(CH_2)_n$- group may contain from one to three heteroatoms independently selected from nitrogen, sulfur or oxygen wherein said $(C_2$-$C_9)$heteroaryl moiety of said $(C_2$-$C_9)$heteroaryl-$(CH_2)_n$- group may optionally be substituted on any of the ring carbon atoms capable of forming an additional bond with a substituent selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms,

$(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl; and

wherein said aryl moiety of said R^3 aryl-$(CH_2)_n$- group is optionally substituted phenyl or naphthyl, wherein said phenyl and naphthyl may optionally be substituted with from one to three substituents independently selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

or R^3 and the carbon to which it is attached form a five to seven membered carbocyclic ring, wherein any of the carbon atoms of said five membered carbocyclic ring may optionally be substituted with a substituent selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl,

H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl; wherein one of the carbon-carbon bonds of said five to seven membered carbocyclic ring may optionally be fused to an optionally substituted phenyl ring, wherein said substitutents may be independently selected from hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms (preferably one to three fluorine atoms), (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-O-(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-(C=O)-O-, (C_1-C_6)alkyl-(C=O)-O-(C_1-C_6)alkyl, H(O=C)-, H(O=C)-(C_1-C_6)alkyl, (C_1-C_6)alkyl(O=C)-, (C_1-C_6)alkyl(O=C)-(C_1-C_6)alkyl, NO_2, amino, (C_1-C_6)alkylamino, [(C_1-C_6)alkyl]$_2$amino, amino(C_1-C_6)alkyl, (C_1-C_6)alkylamino(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$amino(C_1-C_6)alkyl, H_2N-(C=O)-, (C_1-C_6)alkyl-NH-(C=O)-, [(C_1-C_6)alkyl]$_2$N-(C=O)-, H_2N(C=O)-(C_1-C_6)alkyl, (C_1-C_6)alkyl-HN(C=O)-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-(C=O)-(C_1-C_6)alkyl, H(O=C)-NH-, (C_1-C_6)alkyl(C=O)-NH, (C_1-C_6)alkyl(C=O)-[NH](C_1-C_6)alkyl, (C_1-C_6)alkyl(C=O)-[N(C_1-C_6)alkyl](C_1-C_6)alkyl, (C_1-C_6)alkyl-S-, (C_1-C_6)alkyl-(S=O)-, (C_1-C_6)alkyl-SO_2-, (C_1-C_6)alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-(C_1-C_6)alkyl, (C_1-C_6)alkylHN-SO_2-(C_1-C_6)alkyl, [(C_1-C_6)alkyl]$_2$N-SO_2-(C_1-C_6)alkyl, CF_3SO_3-, (C_1-C_6)alkyl-SO_3-, phenyl, (C_3-C_{10})cycloalkyl, (C_2-C_9)heterocycloalkyl, and (C_2-C_9)heteroaryl;

R^4 is hydrogen, (C_1-C_6)alkyl, hydroxy, (C_1-C_6)alkoxy, hydroxy(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C=O)-, (C_3-C_{10})cycloalkyl-(CH_2)$_p$-, (C_2-C_9)heterocycloalkyl-(CH_2)$_p$-, (C_2-C_9)heteroaryl-(CH_2)$_p$-, phenyl-(CH_2)$_p$-, or naphthyl-(CH_2)$_p$-, wherein p is an integer from zero to four; wherein said (C_2-C_9)heterocycloalkyl, (C_2-C_9)heteroaryl, phenyl and naphthyl groups of said (C_2-C_9)heterocycloalkyl-(CH_2)$_p$-, (C_2-C_9)heteroaryl-(CH_2)$_p$-, phenyl-(CH_2)$_p$-, or naphthyl-(CH_2)$_p$- may be optionally substituted on any of the ring atoms capable of supporting an additional bond with a substituent selected from the group consisting of hydrogen, halo, CN, (C_1-C_6)alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-(C_1-C_6)alkyl, (C_1-C_6)alkoxy optionally substituted with one or more fluorine atoms, (C_1-C_6)alkoxy(C_1-C_6)alkyl, HO-(C=O)-, (C_1-C_6)alkyl-O-(C=O)-, HO-(C=O)-(C_1-C_6)alkyl,

$(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$ alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$ amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino $(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

or R^4 and R^5 together with the nitrogen atom to which they are attached form a $(C_2$-$C_9)$heterocycloalkyl group wherein any of the ring atoms of said $(C_2$-$C_9)$heterocycloalkyl group may optionally be substituted with a substituent selected from the group consisting of hydrogen, halo, CN, $(C_1$-$C_6)$alkyl optionally substituted with one or more fluorine atoms, hydroxy, hydroxy-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy optionally substituted with one or more fluorine atoms, $(C_1$-$C_6)$alkoxy$(C_1$-$C_6)$alkyl, HO-(C=O)-, $(C_1$-$C_6)$alkyl-O-(C=O)-, HO-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-O-(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-(C=O)-O-, $(C_1$-$C_6)$alkyl-(C=O)-O-$(C_1$-$C_6)$alkyl, H(O=C)-, H(O=C)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$ alkyl(O=C)-, $(C_1$-$C_6)$alkyl(O=C)-$(C_1$-$C_6)$alkyl, NO_2, amino, $(C_1$-$C_6)$alkylamino, $[(C_1$-$C_6)$alkyl$]_2$ amino, amino$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylamino $(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$amino$(C_1$-$C_6)$alkyl, H_2N-(C=O)-, $(C_1$-$C_6)$alkyl-NH-(C=O)-, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-, H_2N(C=O)-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-HN(C=O)-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-(C=O)-$(C_1$-$C_6)$alkyl, H(O=C)-NH-, $(C_1$-$C_6)$alkyl(C=O)-NH, $(C_1$-$C_6)$alkyl(C=O)-[NH]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl(C=O)-[N$(C_1$-$C_6)$alkyl]$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkyl-S-, $(C_1$-$C_6)$alkyl-(S=O)-, $(C_1$-$C_6)$alkyl-SO_2-, $(C_1$-$C_6)$alkyl-SO_2-NH-, H_2N-SO_2-, H_2N-SO_2-$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylHN-SO_2-$(C_1$-$C_6)$alkyl, $[(C_1$-$C_6)$alkyl$]_2$N-SO_2-$(C_1$-$C_6)$alkyl, CF_3SO_3-, $(C_1$-$C_6)$alkyl-SO_3-, phenyl, $(C_3$-$C_{10})$cycloalkyl, $(C_2$-$C_9)$heterocycloalkyl, and $(C_2$-$C_9)$heteroaryl;

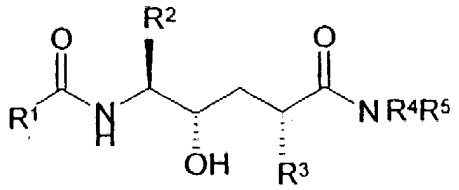
R^5 is hydrogen, $(C_1$-$C_6)$alkyl or amino;

R^6 is hydrogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-$(CH_2)_g$-, $(C_1$-$C_6)$alkoxy(C=O)-$(CH_2)_g$-, $(C_1$-$C_6)$alkyl-(SO_2)-$(CH_2)_g$-, $(C_6$-$C_{10})$aryloxy-$(CH_2)_g$-, $(C_6$-$C_{10})$aryloxy(C=O)-$(CH_2)_g$-, and $(C_6$-$C_{10})$aryl-(SO_2)-$(CH_2)_g$-, wherein g is an integer from 1 to four;

with the proviso that when either R^4 or R^5 is hydrogen, and the other of R^4 or R^5 is $(C_1$-$C_6)$alkyl, R^2 is $(C_3$-$C_{10})$cycloalkyl or isopropyl and R^3 is $(C_3$-$C_5)$alkyl, phenyl, methylvinyl, dimethylvinyl, halovinyl, hydroxy$(C_1$-$C_3)$alkyl or amino$(C_1$-$C_4)$alkyl then R^1 must be other than indol-5-yl, 6-azaindol-2-yl, 2,3-dichloro-pyrol-5-yl, 4-hydroxyquinolin-3-yl, 2-hydroxyquinoxalin-3-yl, 6-azaindolin-3-yl, or optionally substituted indol-2 or 3-yl;

and the pharmaceutically acceptable salts of such compounds.

2. A compound according to claim 1, wherein said compound of formula I has the exact stereochemistry depicted in formula



Ia

wherein R^1, R^2, R^3, R^4 and R^5 are as described in claim 1.

3. A compound according to claim 1, wherein R^1 is optionally substituted pyrazolo[3,4-b]pyridinyl, cinnolinyl, pyridinyl, 6,7-dihydro-5H-[1]pyrindinyl, benzothiazolyl, indolyl, pyrazinyl, benzoimidazolyl, benzofuranyl, benzo[b]thiophenyl, naphthalenyl, quinoxalinyl, isoquinolinyl, 5, 6, 7, 8-tetrahydro-quinolin-3-yl or quinolinyl.

4. A compound according to claim 2, wherein R^1 is optionally substituted pyrazolo[3,4-b]pyridinyl, cinnolinyl, pyridinyl, 6,7-dihydro-5H-[1]pyrindinyl, benzothiazolyl, indolyl, pyrazinyl, benzoimidazolyl, benzofuranyl, benzo[b]thiophenyl, naphthalenyl, quinoxalinyl, isoquinolinyl, 5, 6, 7, 8-tetrahydro-quinolin-3-yl or quinolinyl.

5. A compound according to claim 1, wherein R^1 is optionally substituted pyrazolo[3,4-b]pyridin-5-yl, cinnolin-4-yl, pyridin-2-yl, 6,7-dihydro-5H-[1]pyrindin-3-yl, benzothiazol-2-yl, indol-2-yl, pyrazin-2-yl, benzoimidazol-2-yl, benzofuran-2-yl, benzo[b]thiophen-2-yl, naphthalen-2-yl, quinoxalin-2-yl, quinoxalin-6-yl, isoquinolin-1-yl, isoquinolin-3-yl, isoquinolin-4-yl, 5, 6, 7, 8-tetrahydro-quinolin-3-yl, quinolin-2-yl, quinolin-3-yl, quinolin-4-yl or quinolin-6-yl.

6. A compound according to claim 2, wherein R^1 is optionally substituted pyrazolo[3,4-b]pyridin-5-yl, cinnolin-4-yl, pyridin-2-yl, 6,7-dihydro-5H-[1]pyrindin-3-yl, benzothiazol-2-yl, indol-2-yl, pyrazin-2-yl, benzoimidazol-2-yl, benzofuran-2-yl, benzo[b]thiophen-2-yl, naphthalen-2-yl, quinoxalin-2-yl, quinoxalin-6-yl, isoquinolin-1-yl, isoquinolin-3-yl, isoquinolin-4-yl, 5, 6, 7, 8-tetrahydro-quinolin-3-yl, quinolin-2-yl, quinolin-3-yl, quinolin-4-yl or quinolin-6-yl.

7. A compound according to claim 1, wherein R^1 is optionally substituted quinoxalin-2-yl, quinoxalin-6-yl, quinolin-2-yl, quinolin-3-yl, quinolin-4-yl or quinolin-6-yl.

8. A compound according to claim 2, wherein R^1 is optionally substituted quinoxalin-2-yl, quinoxalin-6-yl, quinolin-2-yl, quinolin-3-yl, quinolin-4-yl or quinolin-6-yl.

9. A compound according to claim 1, wherein R^2 is optionally substituted benzyl.

10. A compound according to claim 2, wherein R^2 is optionally substituted benzyl.

11. A compound according to claim 3, wherein R^2 is optionally substituted benzyl.

12. A compound according to claim 4, wherein R^2 is optionally substituted benzyl.

13. A compound according to claim 5, wherein R^2 is optionally substituted benzyl.

14. A compound according to claim 6, wherein R^2 is optionally substituted benzyl.

15. A compound according to claim 7, wherein R^2 is optionally substituted benzyl.

16. A compound according to claim 8, wherein R^2 is optionally substituted benzyl.

17. A compound according to claim 1, wherein R^3 is optionally substituted (C_1-C_{10})alkyl or (C_3-C_{10})cycloalkyl-$(CH_2)_n$-.

18. A compound according to claim 2, wherein R^3 is optionally substituted (C_1-C_{10})alkyl or (C_3-C_{10})cycloalkyl-$(CH_2)_n$-.

19. A compound according to claim 6, wherein R^3 is optionally substituted (C_1-C_{10})alkyl or (C_3-C_{10})cycloalkyl-$(CH_2)_n$-.

20. A compound according to claim 8, wherein R^3 is optionally substituted (C_1-C_{10})alkyl or (C_3-C_{10})cycloalkyl-$(CH_2)_n$-.

21. A compound according to claim 1, wherein R^3 is optionally substituted n-butyl, t-butyl, 2-methylpropyl, 2-methyl-butyl, 3-methylbutyl, n-pentyl, 2-methyl-pentyl, cyclopentyl, cyclohexyl, 2-methyl-cyclohexyl, or cyclohexyl-methyl.

22. A compound according to claim 2, wherein R^3 is optionally substituted n-butyl, t-butyl, 2-methylpropyl, 2-methyl-butyl, 3-methylbutyl, n-pentyl, 2-methyl-pentyl, cyclopentyl, cyclohexyl, 2-methyl-cyclohexyl, or cyclohexyl-methyl.

23. A compound according to claim 6, wherein R^3 is optionally substituted n-butyl, t-butyl, 2-methylpropyl, 2-methyl-butyl, 3-methylbutyl, n-pentyl, 2-methyl-pentyl, cyclopentyl, cyclohexyl, 2-methyl-cyclohexyl, or cyclohexyl-methyl.

24. A compound according to claim 8, wherein R^3 is optionally substituted n-butyl, t-butyl, 2-methylpropyl, 2-methyl-butyl, 3-methylbutyl, n-pentyl, 2-methyl-pentyl, cyclopentyl, cyclohexyl, 2-methyl-cyclohexyl, or cyclohexyl-methyl.

25. A compound according to claim 1, wherein R^3 is substituted by fluoro or hydroxy.

26. A compound according to claim 2, wherein R^3 is substituted by fluoro or hydroxy.

27. A compound according to claim 21 wherein R^3 is substituted by fluoro or hydroxy.

28. A compound according to claim 22 wherein R^3 is substituted by fluoro or hydroxy.

29. A compound according to claim 23 wherein R^3 is substituted by fluoro or hydroxy.

30. A compound according to claim 24 wherein R^3 is substituted by fluoro or hydroxy.

31. A compound according to claim 1, wherein R^3 is 4,4-difluoro-cyclohexylmethyl, 2-fluoro-2-methyl-butyl, isobutyl, or 1-hydroxy-cyclohexyl.

32. A compound according to claim 2, wherein R^3 is 4,4-difluoro-cyclohexylmethyl, 2-fluoro-2-methyl-butyl, 2-methylpropyl, 2-hydroxy-2-methylbutyl, 2-hydroxy-2-methyl-propyl, or 1-hydroxy-cyclohexyl.

33. A compound according to claim 6, wherein R^3 is 4,4-difluoro-cyclohexylmethyl, 2-fluoro-2-methyl-butyl, 2-methylpropyl, 2-hydroxy-2-methylbutyl, 2-hydroxy-2-methyl-propyl, or 1-hydroxy-cyclohexyl.

34. A compound according to claim 8, wherein R^3 is 4,4-difluoro-cyclohexylmethyl, 2-fluoro-2-methyl-butyl, 2-methylpropyl, 2-hydroxy-2-methylbutyl, 2-hydroxy-2-methyl-propyl, or 1-hydroxy-cyclohexyl.

35. A compound according to claim 16, wherein R^3 is 4,4-difluoro-cyclohexylmethyl, 2-fluoro-2-methyl-butyl, 2-methylpropyl, 2-hydroxy-2-methylbutyl, 2-hydroxy-2-methyl-propyl, or 1-hydroxy-cyclohexyl.

36. A compound according to claim 1 wherein R^4 and R^5 are independently selected from hydrogen, hydroxy, amino, methyl, or ethyl.

37. A compound according to claim 6 wherein R^4 and R^5 are independently selected from hydrogen, hydroxy, amino, methyl, or ethyl.

38. A compound according to claim 8 wherein R^4 and R^5 are independently selected from hydrogen, hydroxy, amino, methyl, or ethyl.

39. A compound according to claim 21 wherein R^4 and R^5 are independently selected from hydrogen, hydroxy, amino, methyl, or ethyl.

40. A compound according to claim 1, wherein said compound is:

7,8-difluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

8-fluoro-quinoline-3-carboxylic acid 1(S)-benzyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-7-fluoro-1-(3(S)-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [4(R)-carbamoyl-1-(2(S)-fluoro-benzyl)-2(S)-hydroxy-7-methyl-octyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4(S)-(2,6-dimethyl-tetrahydro-pyran-4-yl)-2(S)-hydroxy-butyl]-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-5-cyclohexyl-2(S)-hydroxy-4(R)-methylcarbamoyl-pentyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-cyclohexylmethyl-2(S)-hydroxy-7-methyl-4(R)-methylcarbamoyl-octyl)-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-2(S)-hydroxy-4(S)-hydroxycarbamoyl-4-(1-hydroxy-4-methyl-cyclohexyl)-butyl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-(4,4-difluoro-1-hydroxy-cyclohexyl)-2(S)-hydroxy-4-hydroxycarbamoyl-but yl]-amide;

quinoxaline-2-carboxylic acid [1(S)-benzyl-4(S)-carbamoyl-4(S)-(4,4-difluoro-cyclohexyl)-2(S)-hydroxy-butyl]-amide;

quinoline-3-carboxylic acid (1(S)-benzyl-4(S)-carbamoyl-4-cyclohexyl-2(S)-hydroxy-butyl)-amide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiophen-2-ylmethyl-octyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-chloro-2(S)-hydroxy-oct-6-enyl)-amide;

quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S)-hydroxy-5-phenyl-pentyl)-amide;

N-1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-5,6-dichloro-nicotinamide;

quinoxaline-2-carboxylic acid (4(R)-carbamoyl-2(S)-hydroxy-7-methyl-1(S)-thiazol-4(R)-ylmethyl-octyl)-amide;

benzothiazole-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide; or

benzofuran-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-7-fluoro-2(S)-hydroxy-7-methyl-octyl)-amide.

41. A pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases, acute and chronic inflammatory conditions, allergic conditions, infection associated with inflammation, viral, transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity, and granulomatous in a mammal, comprising an

amount of a compound according to claim 1 that is effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

42. A pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by inhibiting MIP-1α binding to the receptor CCR1 in a mammal, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, effective in treating or preventing such disorder or condition and a pharmaceutically acceptable carrier.

43. A method for treating or preventing a disorder or condition selected from autoimmune diseases, acute and chronic inflammatory conditions, allergic conditions, infection associated with inflammation, viral, transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity, and granulomatous in a mammal, comprising administering to a mammal in need of such treatment or prevention an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition.

44. A method for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal, comprising administering to a mammal in need of such treatment or prevention an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating or preventing such disorder or condition.

45. A pharmaceutical composition for treating or preventing a disorder or condition selected from autoimmune diseases, acute and chronic inflammatory conditions, allergic conditions, infection associated with inflammation, viral, transplantation tissue rejection, atherosclerosis, restenosis, HIV infectivity, and granulomatous in a mammal, comprising a CCR1 receptor antagonizing effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

46. A pharmaceutical composition for treating or preventing a disorder or condition that can be treated or prevented by antagonizing the CCR1 receptor in a mammal, comprising a CCR1. receptor antagonizing effective amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/01568

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D215/54 A61K31/47 C07D241/44 A61K31/50 C07D213/82
A61K31/455 C07D217/26 C07D237/28 A61K31/495 C07D307/85
A61K31/34 C07D333/70 A61K31/38 C07D235/24 A61K31/415

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 184 550 A (CIBA-GEIGY AG) 11 June 1986 see page 15, last paragraph; claims 1-3,16,19 --- -/--	1,2,17, 18,21, 22, 25-28, 31,32, 36,39

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
22 May 1998	10.07.98

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hartrampf, G

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/01568

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D241/24 C07D209/42 A61K31/40 C07D277/68 A61K31/425
C07D221/04 C07D213/81 C07D405/12 C07D401/12 C07D409/12
C07D417/12 C07D403/12 C07D471/04 //(C07D471/04,231:00,

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 321 192 A (PFIZER INC.) 21 June 1989 see page 14, line 35 - line 40; example 8 see claim 1 & US 4 923 864 A (ROSATI R.L.) 8 May 1990 cited in the application	1,2,17, 18,21, 22, 25-28, 31,32, 36,39
X	EP 0 374 098 A (CIBA-GEIGY AG) 20 June 1990 see page 3, line 22; claims 1,20,25	1,2,17, 18,21,22

-/--

[X] Further documents are listed in the continuation of box C.

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/01568

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 221:00)

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimumdocumentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 02057 A (SMITHKLINE BEECHAM CORPORATION) 4 February 1993 see claims 1-3,9,10,13,15,16,18; examples 76,88 --- -/--	1-6, 9-14, 17-19, 21-23, 25-29, 31-33, 36,37, 39,41,45

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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Date of the actual completion of theinternational search	Date of mailing of the international search report
22 May 1998	10.07.98

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hartrampf, G

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International Application No
PCT/US 98/01568

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 17003 A (SMITHKLINE BEECHAM CORPORATION) 2 September 1993 cited in the application see claims 1-3,7,9,10	1-6, 9-14, 17-19, 21-23, 25-29, 31-33, 36,37, 39,41,45
X	WO 95 07269 A (NARHEX AUSTRALIA PTY., LTD.) 16 March 1995 see page 26, line 5 - line 36; claims 1,20-23	1-41,45
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A	NATARAJAN S. ET AL. : "Ketomethylureas. A new class of angiotensin converting enzyme inhibitors" JOURNAL OF ENZYME INHIBITION, vol. 2, no. 2, 1988, pages 91-97, XP002065668 see compounds 30,31 and 32 see page 95; table II	1-42,45, 46
A	SAWYER T.K. ET AL.: "Peptidomimetic inhibitors of human immunodeficiency virus protease (HIV-PR): Design, enzyme binding and selectivity, antiviral efficacy, and cell permeability properties" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS , vol. 3, no. 5, 1993, pages 819-824, XP002065669 see compound 8 see page 821; table I	1-42,45, 46

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/01568

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 43,44
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 98/01568

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